BRITISH MEDICAL JOURNAL

LONDON SATURDAY NOVEMBER 15 1958

LATE RESULTS OF OPERATIONS FOR FALLOT'S TETRALOGY

BY

MAURICE CAMPBELL, D.M., F.R.C.P.

From the Cardiac Department, Guy's Hospital, and the Institute of Cardiology, London

Fallot's tetralogy is the most common form of morbus caeruleus: its frequency was mentioned by Peacock in his excellent account in 1866. Its surgical treatment is therefore of great importance, and three methods are now available: (1) subclavian-pulmonary anastomosis or some modification of this; (2) Brock's direct operations of pulmonary valvotomy or infundibular resection or both; and, more recently, (3) open operation with closure of the ventricular septal defect and relief of the stenosis.

This paper describes the results of the first two methods, but I am able to mention my first patient, on whom Sir Russell Brock used the third method in October, 1956. A girl who was aged 4 at the time of her operation, and who was deeply cyanosed and could walk only 30 yards, is now acyanotic and can run about freely with other children, so that symptomatically she could hardly be better. The result, however, is not ideal, for, though her ventricular septal defect seems to have been closed, she still has some stenosis, with a larger heart and right bundle-branch block.

Clearly this third method is the only cure, and will become standard treatment when the present difficulties have been surmounted. The results of anastomotic operations may then be mainly of historic interest, but will serve as a comparison with the results of open operation after another ten years. Valvotomy and infundibular resection will, of course, remain an essential part of any surgical treatment, so that the success they can achieve is of great interest.

Inevitably, as time passes, the child who has had a successful operation for Fallot's tetralogy tends to be compared with the normal child of his age and less with the severely disabled child he was, both by the patient and his parents and by the physician as well. To this extent there is less enthusiasm than at first, and sometimes it needs to be remembered how many patients are leading normal quiet lives at school or at work who previously had no such prospect. This change of attitude is even more important when the patient was only somewhat improved; parents who were delighted at first think mainly of the great disability that remains after a few years.

ANASTOMOTIC OPERATIONS

All types of morbus caeruleus were included in our previous report of the results of 200 anastomotic operations (Campbell and Deuchar, 1953). This makes the conclusions less precise and less easy to follow, so here we are considering only those diagnosed as Fallot's tetralogy: this still includes some where necropsy revealed more complex lesions, but it excludes those with pulmonary atresia or tricuspid atresia where the results are not so good.

After this modification there are 130 patients who obtained good or very good results—127 from the start and 3 from later who were originally classed as "improved" only (see Table I). Those in whom the results of operation were good and those in whom they were very good have behaved in much the same way, and it is simpler to take them together.

TABLE I.—*Early Results of Anastomotic Operations*

	No.	Died at Operation	No Op. Possible	No Improvement	Slight Improvement	Good	Very Good
Fallot's tetralogy ..	165	14	4	5	15−3*	33+3	94
Pulmonary atresia ..	19	6	5	0	3	3	2
Other conditions ..	16	4	2	1	1	3	5
	200	24	11	6	19	39	101

* Three of these subsequently achieved good results, making 130 (94+33+3) whose further progress is considered.

During the period covered in our previous report, up to four years after operation, few of the patients with good results had relapsed. During the subsequent four years we became less satisfied, for several returned to hospital having lost all their improvement. A further follow-up has been more reassuring, for we had seen nearly all those who were doing badly but few of those who were doing well, as they had felt no need to attend hospital.

Of the 130 who obtained good results, we have seen 126 recently or have had reports from them or their doctors. Eight of these (6%) have died and 17 (14%) have lost much or all of their improvement, but 101 (80%) are as good or nearly as good as they were. These have been followed for an average period of over seven and a half years: 11 are well after ten years, 10 after nine years, 28 after eight years, 36 after seven years, and 16 after six years.

Good Results Maintained

Most of these 101 patients have kept all their improvement, though seven have lost some of it—enough for the results to be called good rather than very good. The first 10 patients, most of whom were very disabled before operation (Campbell, 1948), have their cases described briefly to illustrate the results, which were very good in the first five but more varied in the second five. None of them, except Case A5, has an unduly large heart, and all show less

anoxaemia and lower haemoglobin percentages (see Table II), the average of the first five being 104 instead of 136%, though generally they are still a little cyanotic. It is only fair to add that Mr. Alfred Blalock was working at Guy's Hospital and performed some of these first operations, lest others feel that their start was not so successful. The

TABLE II.—*Changes in Heart Size and Haemoglobin Percentage in Patients Who Have Done Well for 9 or 10 Years After Anastomotic Operations*

Case No.	Heart Size (Cardiothoracic Ratio)						Haemoglobin (%)		
	Before Op.	1 Yr.	3 Yr.	5 Yr.	7 Yr.	9 or 10 Yr.	Before Op.	After 4 Yr.	After 9 or 10 Yr.
A1	50	53	53	54	55	55	126	91	110
A2	44	52	53	53	54	53	120	95	98
A3	51	55	55	54	53	52	133	85	114
A4	44	56	55	53	54	54	152	84	103
A5	52	60	65	67	66	65	150	80	95
A13	45	47	48	49	49	50	150	120	122
A16*	52	53	53	52	53	52	130	90	98
A20	47	52	53	53	53	50	110	100	105
A23*	43	48	48	49	50	51	130	85	95
A24	45	53	53	52	52	51	148	95	105
Average	47·3	52·9	53·6	53·6	53·9	53·3	135	93	104
Average of 50 cases	49·8	—	53·9	—	—	53·7	132	104	111
Some More Borderline Cases									
A62	51	51	51	51	48	46	152	110	132
A55	56	55	56	55	55	55	141	120	134
A83	54	59	59	58	57	54	136	127	150

A = anastomosis.

* These two patients were in good health after 9 years but died in the tenth year from cerebral abscess.

ages given are those at the time of operation unless otherwise stated. The prefix "A" indicates anastomotic operations.

Case A1.—A boy aged 7 was enabled to lead a normal life at school except for games. After ten years he can walk five miles and get about his father's farm most of the day, but would find it difficult to earn his living on a farm and is still a little cyanotic.

Case A2.—A boy aged 13; now leads a normal quiet life and is married. For two years he worked long hours in a garage but found this hard, and is now in an accountant's office. His colour looks normal.

Case A3.—A boy aged 3; is now leading a normal school life, except for football. He can walk five miles and can run and play cricket. He has minimal cyanosis.

Case A4.—A boy aged 11 could not walk more than 50 yards, but now walks 10 to 15 miles and his colour is almost normal.

Case A5.—A girl aged 6 could not walk more than 25 yards. After ten years she attends school regularly but has to take things at her own pace. The heart became much larger, but not progressively so.

Case A6.—A girl aged 3 lost her improvement when the anastomosis closed in the seventh year (see below).

Case A7.—A boy aged 7 was very well when his family emigrated to Canada after two years.

Case A8.—A student aged 25 was less disabled than most. He has done well as regards his heart, but has been handicapped by the effects of a cerebral thrombosis after operation and by tuberculosis of the lungs.

Case A9.—A girl aged 5 was greatly improved and the operation probably saved her life, but four years later she was still disabled enough to need a second operation.

Case A10.—A boy aged 3 has continued to do well. In the tenth year he had bacterial endocarditis, but has not lost any ground after it.

Most of these patients were children, who on the whole do best after operation, but some adults do very well. Generally, if patients over 20 can earn their living the obstruction to the pulmonary flow cannot be great, and I have thought it better for them to carry on without operation. However, one man aged 20 who had never worked is now employed regularly as a painter and decorator, and can walk as far as he wants; another, aged 26, is so much better that he sometimes plays football in addition to doing his regular work; both have remained well for six years.

Some patients included among the good results are not as good as the best of these. They cannot do so much and show obvious cyanosis: a doctor seeing them for the first time would diagnose Fallot's tetralogy and might think they needed surgical treatment. Of three such patients, the first is not as well as he was and the other two are still examples of fairly severe Fallot's tetralogy (see bottom of Table II), but it is difficult not to call the results good when two who could not walk 50 yards before operation can now earn a living and the third can attend an ordinary school and walk much further than before.

Case A62.—A boy aged 6 lost some of his improvement after six years and the haemoglobin rose again; but after nine years he is earning his living and can walk a quarter of a mile, instead of 50 yards before operation.

Case A55.—A boy aged 11 was deeply cyanosed and could walk only 50 yards. Nine years later he is doing clerical work and can walk two miles, although his haemoglobin has risen again. He would be better if he had a larger blood flow to the lungs, but his heart might not be able to cope with this, as it has always been rather large.

Case A83.—A girl aged 6 had severe cyanotic attacks and could walk only 400 yards. After operation she could walk two

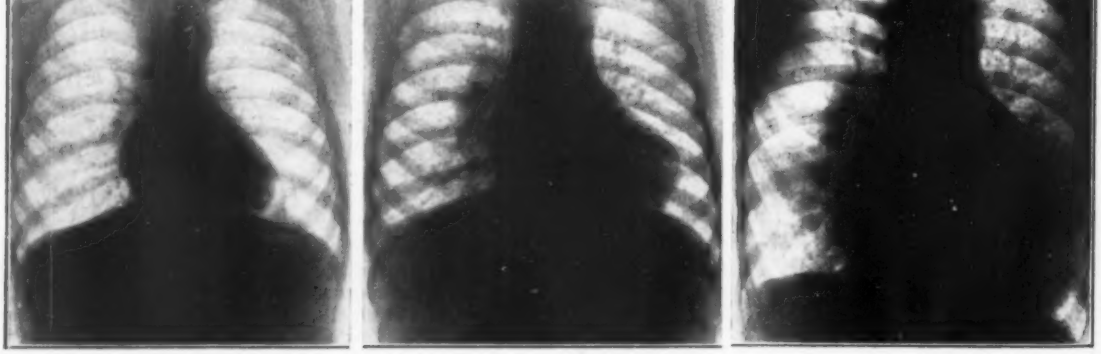


FIG. 1.—Exceptional enlargement of a small heart of a patient with Fallot's tetralogy. Left: Before operation (c.t.r. 48%). Centre: One year after operation, a larger heart (c.t.r. 57%), with lung fields that are much better filled. Right: Nine years after with a very large heart (c.t.r. 70%). She was then well, but died later that year with congestive heart failure. Slight rib-notching can be seen on the fifth right rib from the anastomotic channels from the aorta to the right arm after division of her right subclavian artery and, in retrospect, very slightly even in the radiograph one year after operation. Case A25.

miles and attend an ordinary school, but her colour and her haemoglobin did not improve much. After nine years she is almost as well, but is less contented because she cannot keep up with her friends.

Some patients who obtained a good result as regards their heart are handicapped in other ways. For example, one has some residual disability from post-operative cerebral thrombosis, another from a cerebral abscess, and a third from bronchiectasis. Two are dissatisfied because they are unable to work since leaving school, but this is because they are not intelligent enough to overcome their lack of schooling, and not because the heart has become worse.

Many of the patients are better in summer and can do much less on cold days in winter. Apart from this, any suspicion of deterioration has generally been confirmed by the subsequent course. However, two patients who were thought to be losing ground in the third and fourth years—a period of rapid growth—are as well as ever after seven years.

Good Results Lost

These patients have been divided into three groups: (*a*) those who have died, (*b*) those who have lost all their improvement, and (*c*) those who have lost much of it. The loss is not always due to the anastomosis closing.

Eight Patients Who Have Died

In our earlier report three had died (the fourth included there had tricuspid atresia). When we started this longer follow-up only two more had died, but during the tenth year three who were in excellent health after nine years have died. This may be chance, but shows the need for a long follow-up to get a reliable picture.

Of the three first, a woman aged 20 died suddenly in the street 18 months after operation, no obvious cause being found at necropsy; a girl aged 7 died unexpectedly from pulmonary oedema while on holiday 37 months after operation; and a boy aged 3 died with a cerebral abscess in the third year after.

Of the next two, a boy aged 11 remained well until he had acute nephritis in the sixth year; he recovered, and his blood pressure, which had risen to 170/130, returned to 120/90 mm., but five months later he died at home, probably from a recurrence of the nephritis. Our oldest patient, aged 35, did well for seven years, but then died with carcinoma of the bronchus.

The last three are particularly disappointing, for they had been leading active lives with few symptoms, and when examined nine years after their operation only one had signs that caused any anxiety—anaemia and a large heart; yet they died within a year. Two of them, boys aged 6 and 19, died from cerebral abscesses, both in the tenth year (Cases A16 and A23): the latter had made a good recovery after operation for a cerebral abscess at a different site seven years previously. The last, a girl aged 6, did very well, but her heart became much larger than usual (c.t.r. 47–60%). After nine years it was still larger (Fig. 1), but we hoped part of this was due to her anaemia (haemoglobin 71%) and might be reversed by treatment. Nine months later, however, she was admitted with sudden severe dyspnoea, congestive failure, and anaemia: she seemed to be recovering, but became more breathless and vomited, and died suddenly a few hours later. At necropsy the immediate cause was a mesenteric thrombosis, but she should be regarded as dying from heart failure (Case A25).

Rather surprisingly, none of these patients showed any cardiac deterioration until their terminal illness; we have no reason to think that the anastomosis had closed, and have necropsy proof that it was open in five of the eight. One death from carcinoma of the bronchus was quite incidental and one from nephritis may or may not have been, for we find nephritis rather common in these patients; three were from cerebral abscess; and only three from some form of heart failure.

As the average period of follow-up for all our patients is over seven years, this is a mortality of about 1% per annum. In those who have died the average period after operation was just over three years in four and just under nine years in four.

Loss of All Improvement

Ten other patients have lost all their improvement. When the loss has taken place fairly suddenly—though sometimes in more than one stage—and the continuous murmur can no longer be heard, the reason is clear and in several operation or necropsy confirmed that the anastomosis had closed. This happened in the first five patients shown in Table III, and they reverted to the same state as before operation.

When the loss is gradual it is more difficult to explain in this way, and Case 45 was becoming worse for four years before there was any noticeable change in the continuous murmur: it seems that the stenosis was becoming more severe and that only towards the end was the anastomosis nearly closed. In the last four patients, however, the continuous murmur could be heard as well as before: we think they were showing the natural tendency for the stenosis of Fallot's tetralogy to become more severe, though in some the anastomosis was probably carrying less blood than it had originally.

In all these patients the haemoglobin percentage had risen again—in all but one to about its original level (see Table III). In four of the six where we know about the heart size, it had become smaller again, and in three of these the anastomosis was known to have closed. When the haemoglobin rises to its original level and the heart becomes smaller the anastomosis has probably closed. Short descriptions of these patients follow: four of them have obtained good results after subsequent direct operations.

Case A6.—A girl aged 3 lost nearly all her improvement suddenly after pneumonia in the seventh year. The anastomosis was thought to have thrombosed.

Case A15.—A boy aged 10 did well till he had three epileptiform fits in the fifth year: during the next two years he lost ground and the continuous murmur became inaudible. He died after pulmonary valvotomy, with cerebral softening; at necropsy the anastomosis had closed.

TABLE III.—*Some Details of Patients who Lost All the Improvement Produced by Anastomotic Operations*

Case No.	Anastomosis	Time of Deterioration	Hb Percentage			Heart Size (c.t.r.)			Remarks
			Before Op.	After Op.	Final	Before Op.	After Op.	Final	
A6	Closed	7th year, after pneumonia	157	110	141	49	54	51	2nd op. Good
A15	,,	5th and 6th years	142	109	150	48	50	45	,, Died
A44	,,	7th partly; 9th year all	142	102	130		Erratic		,, Good
A143	,,	5th year during 5 months	100*	105	130	46	48	—	,, ,,
A147	,,	5th year slightly; 6th mainly	143	90	119	41	43	—	,, ,,
A45	Nearly closed	4th to 7th years gradual	117	103	139	54	55	42	,, Died
A40	Open	6th year partly: 7th all, after pneumonia	140	104	148	51	54	57	,, Good
A47	?	? 5th and 6th years	136	—	—	50	—	—	
A54	Open	7th year mainly	100*	101	129	53	56	53	
A82	,,	5th to 7th years, after nephritis	130	108	120	47	47	57	,, Died

* Presumably anaemic.

Case A44.—A girl aged 10 lost some ground in the seventh year. In the ninth year she had to give up her work, having become cyanotic again and having lost all her improvement within a few months: the continuous murmur could no longer be heard.

Case A143.—A girl aged 10 became almost acyanotic and could walk three miles. During the course of five months in the fifth year she lost all her improvement and the anastomosis had closed without any obvious reason.

Case A147.—A girl, aged 16, remained well for five years. After this she became bluer and more short of breath, and some months later had to give up her work: no continuous murmur could be heard.

Case A45.—A boy aged 3 obtained a very good result. In the fourth year his mother thought he was not as well, and by the sixth year there was no doubt about this: the haemoglobin was higher (123%) and the heart was smaller (c.t.r. 48%). His continuous murmur was still as loud, but this was not so in the seventh year, when he had become as disabled and as cyanosed as ever: the heart was even smaller (c.t.r. 42%) and the haemoglobin 139%. A severe high infundibular stenosis was resected, but he died two days later. At necropsy the lumen of the anastomosis admitted a probe only.

Case A40.—A boy aged 8 remained well for six years. Then he could do rather less and his headaches recurred ; some months later he had "pneumonia," after which he lost all his improvement and resumed squatting. It seemed likely that the anastomosis had closed, but the heart had not become smaller and the murmur was as loud as before. There must, I think, have been increasingly severe stenosis, though a year later, when admitted for a direct operation, which was very successful, the continuous murmur could no longer be heard.

Case A47.—A Cypriot boy aged 11 did well for five years. In the sixth year he lost most of his improvement, but we do not know if the continuous murmur can still be heard.

Case A54.—A girl aged 5 lost some ground in the fourth year after a cortical thrombophlebitis, but the result was still good. She lost most of her improvement in the seventh year, mainly in one month. Her smaller heart and higher haemoglobin suggested the anastomosis was closing, but the continuous murmur remained quite loud.

Case A82.—A girl aged 5 remained very well for five years, but then lost ground after scarlet fever and nephritis, and more so during the next two years though the continuous murmur was still loud: her heart became steadily larger, and she often complained of swelling of the ankles and had some albuminuria. She died after an infundibular resection. At necropsy there was nothing to suggest occlusion of the anastomosis before its recent ligation. Her deterioration seems to have been due to increasingly severe infundibular stenosis, the passage having become almost atresic.

Loss of Much Improvement

The anastomotic channel had not closed in any of these seven cases, but, certainly in the first and probably in others, it was carrying less blood to the lungs. In the first two the continuous murmur was less easy to hear. In all except the last, the haemoglobin had increased, and in two (Cases A41 and A120) the heart had become smaller ; by analogy this made us think the anastomosis was closing, but in both it proved to be open at operation. We think, therefore, that many of them were worse because the stenosis was becoming more severe. Some details are given in Table IV. Only two are described briefly, the first as an example of partial thrombosis of her anastomosis at necropsy, and the second as evidence of increasingly severe stenosis.

Case A46.—A girl aged 16 could walk three miles and worked as a telephonist for six years, though before operation trivial exertion provoked cyanotic attacks with unconsciousness. During the sixth to ninth years she lost much of her improvement. Her continuous murmur was heard less easily and her haemoglobin had risen again. She died from cardiac arrest a day after infundibular resection. At necropsy the anastomosis was only partly occluded by a firmly adherent thrombus.

Case A120.—A boy aged 3 lost much, but not all, of his improvement in several stages during the seventh and eighth years. Recently he was taken to America for operation by Mr. Kirklin with an extracorporeal circulation. In spite of the small heart and rising haemoglobin percentage, the continuous murmur was well heard and the anastomosis was found to be functioning well. There was a very severe infundibular stenosis, with an orifice that was almost pin-point, and the ventricular septal defect was large and at the usual site. So far, he is doing well.

Second Operations

Ten of the 17 who lost all or much of the improvement have already had direct operations: six obtained very good results, but the other four died. For some time a direct operation after an anastomotic one that had failed proved disappointing, and the mortality is still much higher than for primary direct operations.

Two other patients have had second operations because their original disability had been so extreme that even after great improvement they still needed more. One has improved greatly, but the second has not benefited.

Progress of 21 Patients who Obtained Little or No Benefit

The four patients in whom no operation was possible, five who were not improved, and 12 only somewhat improved, making 21 in all, can to some extent serve as a control. Eight of these 21 have died. Two proved to have a single ventricle and pulmonary stenosis ; a third died with meningitis, and a fourth with a pulmonary abscess, all within 18 months of operation. These four were reported in our previous paper, and four have died since. One boy who was very disabled and had frequent fits died three years later. One boy, who after two years had a second anastomotic operation that did not help much, died suddenly five years later. One woman, aged 29, gradually relapsed and died five years later. The eighth was in hospital several times with congestive failure, and died with this six years after: her heart was large for an uncomplicated Fallot's tetralogy, and we think she had some additional lesion.

Four patients lost even the slight improvement they had gained at two to six years after operation. This was due to the anastomosis closing. Four others were much the same for three or four years, when they had second operations ; and second operations may be needed in the remaining five, who are much the same after from six to nine years.

In summary, the prognosis of these 21 patients has proved poor. Eight (38%) died after an average period of three years, only three living longer than this. Seven are much the same as before, and six had a subsequent operation, so that the period of follow-up was abridged: two of these had anastomotic operations that did not help much and four had direct operations, of which two proved fatal and two produced good results.

TABLE IV.—*Patients who have Lost Much of the Improvement*

Case No.	Anastomosis	Time of Deterioration	Hb Percentage			Heart Size (c.t.r.)			Remarks
			Before Op.	After Op.	Final	Before Op.	After Op.	Final	
A46	Less	Gradual 6th to 9th years	135	108	122	47	52	52	2nd op. Died
A153	? Less	Gradual 4th year	120	95	118	48	49	50	
A41	Open	6th and 7th years: severe infundibular stenosis ..	128	114	130	50	51	46	2nd op. Good
A61	,,	6th year, after transient hemiplegia	151	116	166	49	51	53	
A108	,,	Gradual 6th and 7th years	157	105	120	54	60	57	
A120	,,	7th and 8th years	150	110	145	51	54	51	Recent op.
A132	,,	8th year, more dyspnoeic and syncopal attacks ..	154	100	90	54	55	55	

It would not be fair to take these as representative of untreated Fallot's tetralogy, because some of them had more complex lesions, and this may have been partly why they did not benefit much from their operations. They do, however, show a striking contrast with the patients who obtained good results.

DIRECT OPERATIONS FOR FALLOT'S TETRALOGY

The results of pulmonary valvotomy and infundibular resection in the first 100 patients operated on by Sir Russell Brock have been reported (Campbell *et al.*, 1954). The operative mortality was 15%; there was little or no improvement in 14%, and a good result in 71%—figures that were not very different from those after anastomotic operations, except that the operative mortality was higher. Our conclusions were based mainly on the 61 patients that had been treated at Guy's Hospital.

We are now reporting a longer follow-up of these 61 patients and adding another 50 operated on in 1953–6, making 111 in all. The operation was mainly infundibular resection in 47, mainly valvotomy in 42, or both procedures in 22 cases. Infundibular resection, which at one time had a higher operative mortality, has now become about the same; but perhaps rather surprisingly it is followed by a good result more regularly; otherwise there was not much difference in these groups, so they have been considered together for most purposes.

Of the 111 patients, 19 died at or soon after operation, 13 obtained little or no improvement, and 79 (71%) obtained good results. None of these 79 has been lost sight of, and they have been followed for an average period of nearly five years—32 for from six to nine years, and all but seven for two years or more.

The operative mortality was higher than for anastomotic operations—17% for all, but 12% for those operated on since 1952. If we exclude 11 who had second operations in which the mortality has been twice as high, it is further reduced to 15 and to 10% respectively. The number with slight or no improvement is 12%—about the same as in the other series. Sometimes this may be because there are other abnormalities that have not been diagnosed or because of some feature that makes surgical correction difficult. Here, too, however, the proportion has been falling in recent years, especially since the fuller realization of the importance of infundibular stenosis even when at first the stenosis appears to be mainly valvular.

Good Results Maintained

Of the 79 who obtained good results, 70 (89%) have remained well during the subsequent years, including most of the earlier patients.

Infundibular Resection

The first eight who had successful results after *infundibular resection* were given in detail in our previous paper, and, partly because I know them so much better than the later ones and know what they can do, their present condition is given briefly (see also Table V).

*Case IR1.**—A girl, aged 13, has kept well for nine years and is now working as a dressmaker, but does not attempt more than this, and leads a quiet home life.

Case IR2.—A young woman, aged 20, is much more active, but her heart is larger (c.t.r. 58%) and she is limited by paroxysmal tachycardia if she does too much.

Case IR3.—A young man aged 19 could do very little, but now is very active and earns his living in Rhodesia. In the ninth year he had bacterial endocarditis, but is able to do just as much after it, though we do not know if his heart, which was still of normal size, has become larger.

*The case numbers are the same as in our previous papers and are the consecutive operations of that particular type. Thus, IR2 indicates the second patient who had infundibular resection without valvotomy. The consecutive V numbers indicate all who had valvotomy with or without infundibular resection as well: they include those with a closed ventricular septum, who are not discussed in this paper.

TABLE V.—*Changes in Heart Size and Haemoglobin Percentage in Patients 7 to 9 Years After Direct Operations*

Case No.	Heart Size (c.t.r.)			Haemoglobin Percentage		
	Before Op.	After 3–4 Yr.	After 7–9 Yr.	Before Op.	After 3–4 Yr.	After 7–9 Yr.
After Infundibular Resection						
IR1	45	49	49	142	110	105
IR2	56	60	58	120	—	102
IR3	47	47	50	130	112	90
IR6	48	52	—	116	93	—
IR7	48	57	54	133	95	102
IR8	47	53	53	128	111	—
IR10	51	54	53	130	95	90
IR20	45	49	48	115	95	95
IR21	49	63	60	105	84	85
IR22	50	53	55	100*	95	100
Average ..	48·6	53·7	53·2	122	103	101
After Pulmonary Valvotomy						
V2	49	56	58	129	126	126
V3	49	53	53	156	110	104
V10	52	53	50	180	110	111
V20	46	52	53	121	128	142
V25	51	56	53	122	105	—
V32	44	48	53	120	105	103
V34	48	52	51	138	118	103
V35	50	54	50	109	85	97
V42	46	50	47	112	95	94
V48	55	57	55	131	96	100
Average ..	49·0	53·2	52·3	132	110	110
Two Patients Who Have Lost their Improvement						
V22	44	46	46	124	108	117
V29	45	49	48	113	97	116

* Presumably "anaemic."

Case IR4.—A boy aged 14 has kept as well for eight years and is prevented from greater activity more by his mental backwardness than by his heart.

Case IR6.—A boy aged 14 is now working as a shop assistant and cycles and plays tennis.

Case IR7.—A boy aged 12 is now working as a telephone operator and can cycle and play cricket.

Case IR8.—A young woman aged 20 was rather slow in getting her full improvement, but now works in a shop and can walk two miles and go dancing.

Case IR10.—A girl aged 7 is exceptionally good after eight years and leads an active life with no obvious cyanosis.

Case IR21.—A girl aged 15 had an exceptionally good result and lost all her cyanosis, but we feared that the pulmonary flow and the heart were too large. Six years later, however, she is leading a very active life and the heart is smaller (c.t.r. 49 to 66%, but 62% after six years).

The results of recatheterization in Cases IR3, IR7, IR8, and IR21 were included in our earlier paper, and the arterial oxygen saturations had risen to 86, 90, 95, and 98% respectively, and the pulmonary flows to 80, 120, 156, and 208% of the systemic flow. It has been suggested that successful direct operations would convert the condition into Eisenmenger's complex. If the underdeveloped outflow tract became completely unobstructed this would be so, but it still provides enough resistance to prevent this; and the last of these four patients is the only one in whom the pulmonary arterial pressure has risen above normal, and then only to 38/12 mm.

Pulmonary Valvotomy

The early patients who obtained good results after pulmonary valvotomy, with or without infundibular resection as well, are nearly as good.

Case V2.—A girl aged 18 is earning her living as a musician though she still shows obvious cyanosis and has to walk slowly.

Case V3.—A girl aged 11 is more active and leads a normal life without obvious cyanosis after nine years. Looking to the future, however, she has T inversion from V_1 to V_6, suggesting right ventricular strain.

Case V10.—A man aged 22 has kept well and at regular work. Even more significant, his haemoglobin has remained about 111% for eight years, although it was 180% with the consequent risk of cerebral thrombosis.

Case V20.—A boy aged 11 was much improved and later could earn his living and walk four miles, although his haemoglobin did not fall. This, as so often, was a correct guide, for in the sixth year he lost some ground and the haemoglobin rose higher than before (see Table V), but he can still work and walk a mile.

Case V25.—A boy aged 9 does everything at school except the more energetic games which he would like to play, but he developed pulmonary regurgitation after operation and the heart became larger. After seven years the regurgitant murmur is still loud, but he is able to do as much and the heart has become smaller again (c.t.r. 51 to 56 to 53%).

Case V32.—A girl aged 18 has maintained all her improvement: she has married and can carry out her household work.

Case V34.—A boy aged 10 has kept well and is working as a laboratory technician.

Case V35.—A boy aged 14 was improved enough to start as a medical student, and, though delayed by tuberculosis of the lung, he is well and working after seven years.

These patients give a representative picture of the results of direct operations. Case V20 has certainly lost some of this improvement, but, like Cases A55 and A83, not enough to prevent one still calling the result good. With increasing experience the surgeon may succeed in producing good results more regularly, but it seems remarkable how often he did so from the start. I do not think many of the later patients are better than these, and indeed it would be hard to be much better than Cases IR3 or V3 or several others. After recent operations there are, however, fewer of the disappointing results that show some improvement but not enough to be called good.

Good Results Lost

Patients Who Have Died

Only 2 of the 79 patients have died. A woman aged 31 was much improved, but died nine months later with Landrey's acute ascending myelitis (Case IR19). A boy aged 9 could walk two miles instead of 100 yards, but in the fifth year he became ill and was thought to have hydrocephalus. At necropsy the brain was flattened by gross dilatation of the ventricles, and the hydrocephalus was attributed to the attack of basal meningitis two years before his valvotomy (Case V51).

Loss of All or Much Improvement

Only two patients have lost all their improvement, but five have lost much of it. Those who have had direct operations are not, of course, exposed to the risk of the anastomosis closing and there is little evidence of re-stenosis at the site of the operation. We think that some patients who have lost ground in both groups are examples of the natural tendency in Fallot's tetralogy for the stenosis to become more severe as the patient gets older.

Short notes about the patients who have lost their improvement follow. The first of these patients, one of the only two who had lost it all, is reported on more fully because the infundibular stenosis must have increased after operation in spite of the larger flow through her pulmonary valve. The sixth girl was beginning to show the effects of her large left-to-right shunt in the same way as Case A25, who died in the tenth year after an anastomotic operation. The seventh and last patient who lost ground (Case V91) seems to have done so because of pulmonary regurgitation.

Case V29.—A girl aged 17 could do a full day's work and go dancing after it: her haemoglobin fell and her heart became larger (see Table V). After "influenza" in the third year she could manage only half-time work. Catheterization showed that the gradient was mainly between the right ventricle (110/0) and the infundibulum (30/0) and only slightly between this and the pulmonary trunk (12/3)—figures much the same as those found at her second operation three years later. She still kept some of her improvement, but in the fourth year she had to give up work and was as bad as ever. Clearly the failure to relieve her infundibular stenosis meant that the operation had been incomplete, but the great improvement for three years and its subsequent loss show that this must have become worse and it was found to be very severe when subsequently she had a successful infundibular resection.

Case V22.—A girl aged 12 had an excellent result and could lead a normal life, sometimes walking as far as nine miles. After "influenza" in the fifth year she could walk no more than a mile. In the sixth year she became worse again and was little, if any, better than at the start.

Case IR25.—A boy aged 9 could walk a mile and attend school regularly. In the fifth year he could not get about so well, and his haemoglobin had risen from 104 to 119%.

Case IR41.—A boy aged 2 was so disabled with frequent attacks of unconsciousness that pulmonary atresia seemed likely. He became much better, both in colour and in capacity, and this lasted for two years. After this he could not walk more than 50 yards and squatted more often, though the attacks of unconsciousness did not recur.

Case V113.—A boy aged 5 was much improved, though he still squatted sometimes. After five years he could not do so much and his heart was smaller (c.t.r. 52 instead of 57%), but this may have been due to the growth of his chest. This patient and the next one had infundibular resection as well.

Case V117.—A girl aged 9 could walk only 50 yards. After open cardiotomy she was greatly improved and lost all her cyanosis, but the heart enlarged more than usual (c.t.r. 48 to 60%). Four years later she still seemed well, but her lungs were pleonaemic with a hilar dance and the heart was still as large. She was more dyspnoeic, and sometimes after doing too much was orthopnoeic at night

Pulmonary Regurgitation

This has proved a less important complication than was feared—much less important with pulmonary than with aortic valvotomy, presumably because the relevant pressures are so much lower and the valve is rarely calcified. Pulmonary regurgitation of significant degree has occurred in three patients. In the first (Case V25) and in the second it did not seem very important, but in the third it was.

Case V60.—A boy aged 7 has maintained his good result for six years, but his heart has stayed larger (c.t.r. 48 to 57%).

Case V91.—A girl aged 12 was greatly improved after operation, but developed pulmonary regurgitation. A year later, after pleurisy, she became increasingly dyspnoeic. After another year she was readmitted with a loud pulmonary diastolic murmur, a raised venous pressure, and a greatly enlarged liver; her heart had become enormous (c.t.r. 51 to 71%). With rest, salt restriction, digitalis, and mersalyl she improved, but it seemed that she would be permanently disabled. She gradually improved, however, and a year later was able to stop all treatment except digitalis and to resume work as a dressmaker, though her liver was still palpable: her heart has become smaller again (c.t.r. 64%). In retrospect it seems that she might have had some infection with a pericardial effusion, but there was no other evidence of this.

OBJECTIVE EFFECTS OF BOTH OPERATIONS

The success of these operations has been judged subjectively by the improvement in the patient's capacity and colour. This is the best way when the doctor knows his patients well, for it measures the essential change. In our earlier follow-up there was good correlation between this subjective judgment and the objective changes in the polycythaemia and haemoglobin percentage. The more important findings—the continuous murmur, squatting, the haemoglobin percentage, and the size of the heart—are now discussed. All these, except the first, apply equally to anastomotic and to direct operations.

Physical Signs.—An easily heard continuous murmur indicates a good flow through the anastomosis. If it becomes more difficult to hear, the flow to the lungs is smaller and it is likely to become inaudible: then there are generally other reasons for thinking that the anastomosis has closed. A large flow will often produce some increase in the pulse pressure, but a patient may obtain a very good result without this, and an easily heard continuous murmur is generally a more useful sign. The auscultatory signs are not much use in judging the results of direct operations, and it is still possible to diagnose some stenosis in most of the successful cases; further, a loud murmur may be due to the irregularity of the outflow tract after operation rather than to the severity of the obstruction.

Squatting.—When the result is good the patient ceases to squat: it is surprising that a habit so long-established should be stopped so suddenly. Patients forget about it and may seem surprised when they are questioned on it. Older patients may, however, force themselves to stop squatting for social reasons, so its absence is not always reliable. Resumption of the habit always means that the patient has become worse and often that he has lost all his improvement.

Haemoglobin Percentage and Polycythaemia.—A fall towards normal in the haemoglobin percentage and in the red-cell count is generally a reliable sign of a better blood flow to the lungs and of less anoxaemia. They will, of course, fall if the patient becomes anaemic from loss of blood or otherwise, and then he is worse off. Sometimes the real degree of anoxaemia is more severe than is suggested by the relatively small increase of haemoglobin, because the patient is "anaemic": a red-cell count that is high in relation to the haemoglobin percentage will often give an indication of this. Otherwise, any subsequent rise is a reason for thinking the patient is not as well as before.

In our earlier series the mean haemoglobin of all the patients with good results fell from just under 130 to 103%, and the fall was almost the same for anastomotic as for direct operations. The percentage was generally between 120 and 159 before operation and between 90 and 119 after it, though there was, of course, a wide range.

Most of the patients with good results have maintained this improvement in their colour and in their blood count. In some, however, who have not lost their improved capacity the haemoglobin has risen above the lowest level to which it had fallen. There is more evidence of this after anastomotic than after direct operations. In 50 cases of the former the average haemoglobin fell from 132 to 104% after three to four years, and had risen to 111% after eight to ten years. In 20 cases after direct operations it fell from 127 to 107% after three to four years, and was still 106% after seven to nine years, but the difference is small. It could be explained by the anastomosis becoming somewhat smaller or even by its failing to grow as much as the patient.

A rise of haemoglobin to near the original level is one of the most reliable signs that the patient is not doing well, and often means that the anastomosis has closed (see Table III).

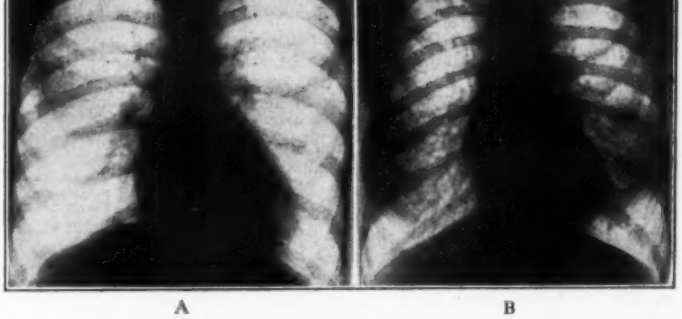
The electrocardiogram is not very useful in judging the result. The right ventricular preponderance is not likely to diminish, for the right ventricle is still working against the same high pressure, and the patient's increased activity must increase the work of the right side, and, sometimes perhaps after anastomotic operations, of the left side of the heart as well. There is some tendency, as the years pass, for the T inversion and the signs of right ventricular strain to increase, but the patients with these signs are not showing any harmful effects from them so far. If patients escape the other hazards of Fallot's tetralogy, right-sided failure seems likely to follow some time in the near future, but over the ten-year period this has not been important.

Changes in the Size of the Heart

The increase in the size of the heart after anastomotic operations was noticed almost at once, and at first there was some fear that this might be progressive and lead to heart failure. The same increase occurs after direct operations. We found that the average change in the cardiothoracic ratio was from 50 to 53% after anastomotic operations and from 48 to 52% after direct operations, with the same wide range of variation after both, and that the increase had generally reached its maximum a month or two after operation and was not progressive (Campbell and Deuchar, 1953; Campbell *et al.*, 1954).

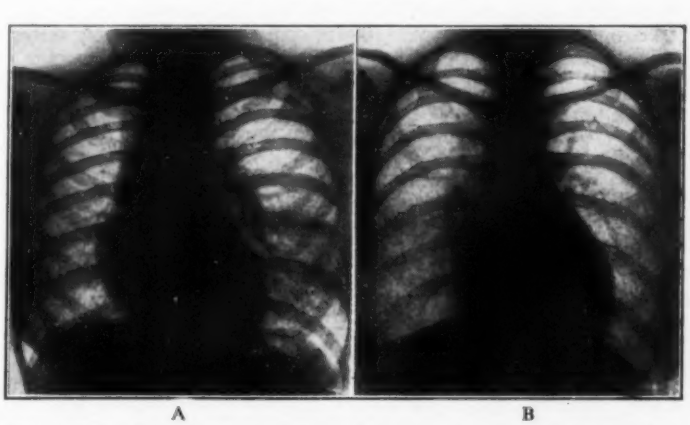
Our observations on the size of the heart in this longer follow-up are not so complete, but include nearly all those who have been followed for from 8 to 10 years. Many of the figures given in Tables II and V show that up to 10 years the increase is rarely progressive and the average size after 8 to 10 years is much the same as after three to four years. Where figures are available the average increase in the cardiothoracic ratio is rather less than one-tenth (from 49 to 53.5% after three to four years and to 53% after 8 to 10 years), and this is the same after anastomotic and after direct operations. These average figures hide large individual variation, as is shown in the Tables, and even in patients with very good results the increase may be less than this or much more.

In Fallot's tetralogy the heart is often small and undeveloped, partly, perhaps, from lack of use. Some increase in its size must be expected if the patient is to have an



A B

FIG. 2.—More usual heart size in two patients nine years after successful operations for Fallot's tetralogy. Both had equally good results clinically, but the increase in the blood flow to the lungs is more obvious in one than in the other, where the lungs are still oligaemic. (A) C.t.r. 51% (12/23.5 cm.) Case A24. (B) C.t.r. 51% (13.5/26.5 cm.) Case A23.



A B

FIG. 3.—Teleradiograms of two patients eight years after anastomotic operations for Fallot's tetralogy. Generally the two lungs seem equally filled, but from the better filling of one lung it is easy to see that the operation was on the left side in one (Case A133) and on the right side in the other (Case A34). The left pulmonary artery was unusually large in A before operation. Both results are extremely good, and the hearts are not unduly enlarged (c.t.r. 54%).

adequate pulmonary blood flow and is to lead a more active life. An increase of one-tenth in the cardiothoracic ratio where it was 45% before operation leaves it of normal size and has no drawbacks, and where it was 50% the same increase leaves it still only slightly enlarged. Examples of both these degrees are given in Figs. 2 and 3. We have no anxiety about an increase to 55 or even 57% unless, as is unusual, it is progressive. With figures over 60% we are more anxious, and such a size is, of course, reached more easily if the heart was large before operation. Patient A25, who was notable from the start as showing pleonaemic lungs and one of the largest hearts (see Fig. 1), illustrates the risk, for she died in the tenth year with congestive heart failure, and we are anxious about the outlook for Case V117. Sometimes, however, the heart may become rather smaller as it becomes habituated to the new conditions, both after anastomotic and after direct operations (see Cases A5 and IR21).

DISCUSSION

Many authors have published their results after operation, but there are few long follow-up studies. The recent one of Taussig and Blalock's cases by White *et al.* (1956) is most valuable, but only 73% of the 500 cases had been traced. Of the 212 patients with Fallot's tetralogy who obtained a good result, 69% have kept this for from five to eight years, 20% have lost ground, and 11% have died during this period, but this is reduced to 9% if second operations are excluded. The great value of successful operation is shown by the contrast of this mortality with one of 44% among those who obtained only fair results from operation. In our series there is a similar contrast with rates of 6 and 38% respectively.

The best age for operation seemed to be between 8 and 12 years, for here the number who had maintained good results reached over 80%. The effect of age, however, is not great in our series, for the figure was 80% in each five-year period except in infants and in those over 20, where the results were less good originally and less well maintained afterwards.

Bacterial endocarditis had occurred in 6% of their series, about 1% per annum, but only 1 in 15 of these patients died. This incidence is higher than in our series, but for cerebral abscess it is much lower than ours. Few of the 33 deaths were due to heart failure; seven were after a second operation and the remainder from a variety of causes.

Potts's Aorto-pulmonary Anastomoses.—The immediate results are not very different from other anastomotic operations—an operative mortality of 9% and a good result in 68%. Only three of my patients have had this variety. Potts *et al.* (1955) have followed up their first 100 cases for about the same period as we have, and find that good results have been maintained at least as well as after other anastomotic operations: there were five deaths—one from a heart attack, one from a brain abscess, one from rheumatic fever, and two from "pneumonia" which may have been partly pulmonary congestion from too large a flow. Though it is not easy to compare the exact degree of enlargement of the heart, it seemed generally to be rather greater, but again was not often progressive.

Comparison of Anastomotic and Direct Operations

No other follow-up study of a large series of patients after direct operations has been found, and in any case it seems better to compare our own patients, who have so far as possible been assessed in the same way. Scientifically, it would have been better if direct operations had been started at the same time and done alternately, but this was not possible. All these anastomotic operations were done in 1947–51. Most of the direct operations were done in 1949–52, but some up to 1956. The selection depended mainly on Sir Russell Brock's view of what was the best surgical procedure at the time, but the earlier patients were, I think, generally the more severe.

The results of direct and anastomotic operations were very similar in our earlier reports, except that the former had a higher operative mortality. This longer follow-up makes them more equal, for there are fewer deaths and fewer complete relapses after direct operations. We thought from an early stage that they more often relieved all the cyanosis, and this is also the view of Wood (1956), but the average reduction in the polycythaemia and haemoglobin level was the same at first and is only a little better maintained after direct operations. The degree of improvement is, however, more varied, from slight or moderate improvement to good or very good results according to the degree of success of the pulmonary valvotomy or infundibular resection. Successful anastomotic operations, on the other hand, tend to produce a more uniform degree of improvement, since the extrapulmonary blood flow through the subclavian anastomosis will generally be proportional to the body size.

The patients who obtained good results but later died or lost ground after each type of operation have been described. Good results have been maintained in 80% after anastomotic and in 89% after direct operations, and this means that the patients were able to work or attend an ordinary school. Allowing for the different length of the follow-ups, the figures for direct operations are not much better, but the real advantage is greater, for the annual death rate and the proportion losing all improvement are only half those after anastomotic operations, the totals being made nearer equality by the larger number who lost only some improvement (see Table VI). It is, however, a more severe test for the latter, because there have been several relapses and deaths during the tenth year, a period that has not yet been reached by many who had direct operations.

TABLE VI.—*Results of Anastomotic and Direct Operations Compared*

Operation	Total No. With Good Results Traced	Subsequent Progress				Annual Loss (Percentage)			
		Good Results Maintained	Died	Lost All Improvement	Lost Much Improvement	Died	Lost All Impr.	Lost Much Impr.	Total
Anastomotic	126	101	8	10	7	0·9	1·1	0·7	2·7
Direct ..	79	70	2	2	5	0·5	0·5	1·4	2·4

The loss of all improvement after anastomotic operations generally occurred because the anastomosis had closed. Sometimes, however, and more often when only some improvement was lost, it seemed due to the natural tendency for the stenosis to become more severe; and this is probably the main reason for the deaths in childhood of those who have not had operations.

None of the *deaths* was due to the anastomosis closing, except indirectly, when it led to their needing second operations. About one-third were due to heart failure in some form, and probably this was at least hastened by the increased activity of the patients; about one-third were due to incidental causes; and the remaining third to cerebral causes, mainly cerebral abscess.

Cerebral abscess is a well-known complication of Fallot's tetralogy, and we have discussed the reasons (Campbell, 1957). Even so, among 130 patients, three dying from cerebral abscess* and three others making good recoveries after operations for it is a high proportion. We do not think it has any connexion with the anastomosis, except in the broad sense that the patients could lead more active lives with the consequent exposure to fatigue and infection. It is all the more remarkable since during the same period of follow-up only four of these patients suffered from

*Since this was written, two more patients, a boy aged 15 and a girl aged 4, both of whom did well for seven years after anastomotic operations, have died with cerebral abscesses and both in the eighth year after operation. Of the 10 patients who have died, five died with cerebral abscesses.

bacterial endocarditis : all recovered and were no worse afterwards.

So far, no patient who had a successful direct operation has died with a cerebral abscess. A girl aged 3 who was only improved died with convulsions in the second year after pulmonary valvotomy ; at necropsy the posterior cusp of a valve that was bicuspid had been split, and a large area of the brain supplied by the middle cerebral artery was necrotic (Case V96). This supports the view that a cerebral abscess may develop from a primary thrombosis (Campbell, 1957), but in this case the thrombosis was so extensive that it led to her death before this could happen.

Future Outlook

Even after a successful operation there is still Fallot's tetralogy, though in a slight rather than a severe form. A larger proportion will reach the stage that one sees occasionally without operation, subjects who can lead a quiet life up to 40 or 50 years. Bedford (1956) reported two such patients whom he had observed for 27 years. One, who died when she was 52, had got on tolerably well until the last four years of her life, when she developed slight congestive failure and cerebral symptoms with increasing cyanosis and dyspnoea. The other was still without failure when she was 52 : her haemoglobin had been up to 170% and her cerebral symptoms were relieved from time to time by venesection. White and Sprague (1929) described the well-known example of longevity—the composer Henry Gilbert, who died when he was nearly 60. Marquis (1956), in an important paper on the longevity and the early history of the tetralogy of Fallot, described the case of a woman who lived to the age of 64.

Our oldest patient is now 53: though cyanosed from birth and squatting frequently as a child, she could lead a quiet life at home but could not go to work. Since the age of 48 she has been more breathless and can walk only 100 yards, and, though she has had a large heart (c.t.r. 63%) and gross right ventricular strain with T inversion from V1 to V4 and congestive failure, is losing ground only slowly.

It is possible now to estimate how many of the patients who have had a successful operation are likely to be reasonably active till middle age. Assuming that the number losing ground will continue at the same rate and that the mortality among those who have lost their improvement will be much higher (38% in seven years), a rough forecast of the position after 7, 14, and 21 years, based on our figures for anastomotic operations, is given in Table VII.

TABLE VII.—*Estimated Condition of 100 Patients Who Have Had a Successful Operation for Fallot's Tetralogy*

	Patients Who Will Have Died	Patients Severely or Moderately Disabled	Patients Leading a Satisfactory Quiet Life
After 7 years	6	14	80
,, 14 ,, ...	17 (6+6+5)	19 (14−6+11)	64 (80−16)
,, 21 ,, (average age 31·5 years)	29 (17+8+4)	20 (19−8+9)	51 (64−13)

We think that half the patients who obtained good results will be reasonably well after 21 years, but the average age will still be only about 31 years. Perhaps one-quarter will be able to carry on in this way till they are 50 ; but this is even more speculative, and is mentioned only in the hope that someone will prove or disprove it by following the patients for another twenty years. The proportion maintaining their good results after direct operations should become relatively higher as the years pass, for, so far, fewer have died or lost all their improvement. The number of these patients who are able to work and enjoy life in a way that was impossible before is even more important than the prolongation of life.

SUMMARY AND CONCLUSIONS

Some of the patients who obtained a good result after an anastomotic or after a direct operation for Fallot's tetralogy have lost all or part of their improvement during the subsequent 8 to 10 years. Often this is due to the inevitable risks of the condition, for all these patients still have Fallot's tetralogy, though the stenosis has to some extent been relieved, directly or indirectly. These causes, especially cerebral complications, were responsible for more than a third of the deaths ; the heart could not support the increased pulmonary flow and the increased activity that it allowed in another third ; but in the final third the cause was not directly related to the heart condition or to the operation. In many patients who lost all their improvement after anastomotic operations, however, this was due to the anastomosis closing. In others, and in most of those who lost some of their improvement after both sorts of operations, it seemed to be due to the tendency for the stenosis to become more severe.

Of those who obtained good results, 80% have maintained them for an average period of seven years after anastomotic operations and 89% for five years after direct operations. The long-term advantage of the latter is greater than appears from these figures, for there were only half as many deaths and half as many who lost all their improvement with direct as with anastomotic operations. We think that perhaps half of those who obtained good results may be reasonably well 20 years after operation.

After anastomotic operations, increasing difficulty in hearing the continuous murmur is a bad sign, and if it cannot be heard the anastomosis has probably closed. The auscultatory signs after direct operations are not so much help.

The reduction in the anoxaemia and resultant polycythaemia and high haemoglobin percentage that was found three or four years after operation has been maintained in most patients for the six to ten years of this longer follow-up, but not, of course, in those who had lost their clinical improvement.

The heart increases in size within a few weeks after a successful anastomotic or direct operation. On the average the cardiothoracic ratio increases by one-tenth (49 to 54%) and remains at this level for 8 to 10 years. There are no drawbacks to some increase in the size of the smaller hearts. The ideal is a limited increase, large enough to indicate a reasonable pulmonary flow that will enable the patient to do more, but not large enough to throw an undue strain on the heart, and this is generally about 10% : it is unlikely to be progressive and there is no reason to be anxious about it. In fact, if a heart that has become larger returns to near its original size, especially if the haemoglobin returns to its original level, the anastomosis has probably closed or the increased pulmonary flow has been lost by the stenosis becoming more severe.

Neither of these operations for Fallot's tetralogy is curative, for, of course, the ventricular septal defect remains and the right ventricle is working against the systemic pressure. These results show, however, that generally they produce great improvement that lasts for many years. The good results after direct operations suggest that when the ventricular septal defect can be closed it should not be difficult to relieve the infundibular or valvular stenosis.

It is a pleasure to thank Sir Russell Brock, not only for his outstanding work in developing these direct operations, but for allowing and even encouraging me to judge the success of his results; also Dr. Charles Baker for his help and for the inclusion of some of his patients; and Mr. Holmes Sellors and Mr. Ian Hill for operating on some and for keeping me so well informed about what they had done. I also thank Drs. S. S. Suzman, Geoffrey Reynolds, and D. C. Deuchar for help at different stages in the follow-up of so many patients for up to ten years, and Drs. Deuchar, R. J. Shephard, and L. Brotmacher and the registrars at the National Heart Hospital for the results of catheterization.

REFERENCES

Bedford, D. E. (1956). *Proc. roy. Soc. Med.*, **49**, 314.
Campbell, M. (1957). *Lancet*, **1**, 111.
—— (1948). *Guy's Hosp. Rep.*, **97**, 1.
—— and Deuchar, D. C. (1953). *Brit. med. J.*, **1**, 349.
—— —— and Brock, R. (1954). Ibid., **2**, 111.
Marquis, R. M. (1956). *Brit. med. J.*, **1**, 819.
Peacock, T. B., (1866). *On Malformations of the Human Heart*, 2nd ed. Churchill, London.
Potts, W. J., Gibson, S., Berman, E., White, H., and Miller, R. A. (1955). *J. Amer. med. Ass.*, **159**, 95.
White, B. D., McNamara, D. G., Bauersfeld, S. R., and Taussig, H. B. (1956). *Circulation*, **14**, 512.
White, P. D., and Sprague, H. B. (1929). *J. Amer. med. Ass.*, **92**, 787.
Wood, P. (1956). *Diseases of the Heart and Circulation*, 2nd ed. Eyre and Spottiswoode, London.

VACCINATION AGAINST POLIOMYELITIS WITH LIVE VIRUS VACCINES

4. A REVIEW OF THE PRESENT POSITION

BY

G. W. A. DICK, M.D., D.Sc., F.R.C.P.Ed.
Professor of Microbiology

AND

D. S. DANE, B.A., M.B., B.Chir.
Lecturer in Microbiology

The Queen's University, Belfast

In a report recently published by the World Health Organization (1958), the Expert Committee on Poliomyelitis strongly recommended that controlled field trials of live attenuated poliovirus vaccines should be carried out. The committee suggested suitable circumstances and populations for the trials and specified the strains of virus which it considered should be used. Trials are now in progress in many parts of the world, and a preliminary report of one of them has already been published (Courtois, Flack, Jervis, Koprowski, and Ninane, 1958). The purpose of this review is to give the reader who is unfamiliar with the subject some idea of the progress that has been made in the development and testing of attenuated poliomyelitis vaccines.

The possible advantages of living attenuated poliovirus vaccines over formalinized vaccines (Salk type) are that they can be given by mouth, that they are cheaper to produce, and that they may give a better immunity. They certainly give a broader type of immunity which will for a time prevent or modify subsequent infection of the alimentary tract with poliovirus. This is in contrast to the immunity at present produced by vaccination with formalinized vaccines which does not modify subsequent alimentary infection, at any rate to the same degree. The difference in the immunity produced by the currently available formalinized vaccines and attenuated virus vaccines is important because the use of attenuated virus vaccines in a community might interfere with the natural spread of virus, and so far there is no evidence that formalinized vaccine is capable of doing this (Langmuir, 1957; Fox, 1957a, 1957b).

In the last few years there have been a number of small laboratory-studied trials of attenuated poliovirus vaccines, and there has been much progress in their development (Sabin, 1957a, 1957b), but the rapid emergence of a successful formalinized vaccine in 1955 removed some of the urgency which might have led to their earlier trial in the field. This delay allowed time for cautious progress, which may have been a good thing because attenuated poliovirus vaccines have certain novel features not previously encountered in human vaccines.

The poliovirus strains incorporated in current living vaccines developed by Sabin (1957b), by Cox and his associates (see da Silva, McKelvey, Bauer, Prem, Cooney, and Johnson, 1957), and by Koprowski (1957) have all been grown in monkey-kidney-tissue culture and selected for their comparative lack of neurotropism when inoculated into the C.N.S. of monkeys in large amounts. The vaccine viruses are given orally and cause an inapparent infection. They multiply in the alimentary tract like natural polioviruses, and the vaccinated subjects develop an immunity which is probably similar to that following an infection with one of the less invasive naturally occurring strains.

Attenuated poliovirus vaccines, like any other vaccines, require testing in the field for safety and effectiveness, both to the individuals vaccinated and to the community as a whole. For reasons of clarity these different aspects are considered separately.

Safety to the Vaccinee

The safety of attenuated poliovirus vaccines to vaccinees has been assessed both by direct clinical observation and, indirectly, by studying alterations which may occur in the character of the vaccine virus after multiplication in the human host.

To the best of our knowledge no illness definitely attributable to the use of attenuated poliovirus vaccines has so far been reported among thousands of persons who were observed carefully after vaccination in different trials with several different attenuated virus vaccines. This is a most encouraging fact, but we must bear in mind that nearly all natural poliomyelitis infections are mild or inapparent, especially with types II and III poliovirus, and that many of the people vaccinated in these trials have either been immune before vaccination or have been selected in a manner which has been far from ideal.

The indirect assessment of safety is made by testing the properties of the virus excreted by vaccinees. While there is a wide spectrum of monkey neuropathogenicity among naturally occurring or *wild* polioviruses, markedly neurotropic strains have always been recovered from the faeces of paralysed patients. If the excreted vaccine virus remains considerably less neurotropic for monkeys than wild polioviruses, which have been isolated from the faeces of paralytic cases, then it is usual to presume that the vaccine virus will do no harm to the vaccinee.

So far only one vaccine virus has been shown to change greatly in its neurotropism after growth in the human gut (Dane, Dick, Connolly, Fisher, and McKeown, 1957). This was the rodent-adapted TN type II poliovirus (Koprowski, Norton, Jervis, Nelson, Chadwick, Nelsen, and Meyer, 1956), and there is general agreement that it is unsuitable for further trial (Dick and Dane, 1957; World Health Organization, 1958). All the other vaccine viruses which have been grown in monkey-kidney tissue culture and have been tested have shown some change towards greater neurotropism, but these changes have been insufficient to cause anxiety for the safety of vaccinees. If safety for the individuals receiving vaccine were all that was required of a vaccine, then there would be few problems in planning progressively larger trials of the currently available attenuated strains, though opinions would vary on the relative importance of direct clinical assessment and the indirect laboratory

study of excreted virus; and they would also vary on the degree of neurotropism theoretically permissible in the attenuated virus.

Unfortunately the vaccine viruses now undergoing trials have been shown on numerous occasions to spread from vaccinees to their associates. Spread has not always occurred, but neither does it always occur with natural poliovirus infections. Because of this ability to spread by contact infection we have to consider carefully the safety of the vaccine viruses to the community in which they are used.

Safety to the Community

The spread of a poliomyelitis attenuated vaccine virus from vaccinees to their contacts was first demonstrated by Koprowski *et al.* (1956) with SM type I virus. His subjects in this trial were incontinent institutional children. Later we demonstrated that SM virus could spread in a normal household (Dick, Dane, Fisher, Connolly, and McKeown, 1957). With the more recently developed attenuated polioviruses spread of virus from vaccinees to their contacts has been shown (Paul, Horstmann, Melnick, Niederman, and Deutsch, 1957; da Silva *et al.*, 1957; Smorodintsev, Drobishevskaya, Gorev, Ilienko, Kluchareva, and Kurnosova, 1958; Smorodintsev, personal communication). To date no significantly greater change towards neurotropism has been reported for virus recovered from infected contacts than has been observed in the excreted virus of some vaccinees. This finding is satisfactory, but the number of observations has necessarily been limited by the number of monkeys which are required for this type of test.

The basic problem we have to consider is the safety of the virus which is excreted by vaccinees and which will probably spread to other members of the community. As stated earlier, there is a broad spectrum of neurotropism among wild polioviruses. From the evidence so far published we do not consider that the virus excreted by some vaccinated subjects in recent trials can be differentiated from the less neurotropic strains of wild poliovirus. This opinion is based on our own interpretation of results from other laboratories, and we realize that not everyone will agree with it. Further work may show that there has been an irreversible change in the vaccine virus and that the excreted viruses are in fact unlike wild polioviruses and are never likely to change sufficiently to become dangerous. At the moment we consider that the irreversibility of the change is not proved.

If we accept that excreted vaccine polioviruses are similar to wild avirulent polioviruses, then how safe are they? Because neurotropic strains of virus have always been isolated from paralytic cases we may presume that the avirulent wild strains are probably safe provided that they are stable and cannot change to a more neurotropic form. Unfortunately there is little information on the stability of wild polioviruses, and for this reason we have been attempting to discover more about the problem by comparing the monkey neurotropism of polioviruses isolated from the faeces of paralytic patients and their close contacts. This method of approaching the problem is open to the criticism that, however carefully one may select a case and a contact, there is never absolute proof that both were infected with the same virus strain. The results of tests on three pairs of viruses are shown in the Table. Faecal virus was given one passage in monkey-kidney-tissue culture and then inoculated intracerebrally into rhesus monkeys in various amounts.

Comparison of the Monkey Neurotropism of Viruses Excreted by Paralysed Children and their Contacts

Serial Letter of Pair	Initials of Children	Type of Infection	Monkeys Paralysed when Inoculated with the Following TCD_{50} of Virus				
			10^6	10^5	10^4	10^3	10^2
A	D.D.	Paralytic	3/3*	3/3	3/3	1/3	0/3
	P.B.	Asymptomatic	1/3	1/3	0/3	0/3	—
B	J.A.	Paralytic	—	—	3/3	3/3	3/3
	R.Y.	Asymptomatic	3/3	3/3	3/3	—	—
C	W.N.	Paralytic	—	—	2/2	—	—
	K.S.	Minor illness	—	—	2/2	—	—

The techniques used in these tests are fully described elsewhere (Dane, *et al.*, 1957).
* Denominator = number of monkeys inoculated. Numerator = number of monkeys paralysed.
— Indicates not tested.

With two pairs (B and C) the viruses isolated from both the contact and the paralytic case were probably equally neurotropic. But in pair A, though the virus from the paralytic case (D.D.) was highly neurotropic, the virus from the contact (P.B.) was only slightly neurotropic and fell into the group of naturally occurring avirulent strains. The virus from P.B. resembled in monkey neurotropism (as judged by intracerebral inoculation) the virus excreted by subjects vaccinated with SM 100 type I poliovirus vaccine (Dick *et al.*, 1957; Koprowski *et al.*, 1956) and by subjects vaccinated with more highly attenuated poliovirus strains in a recent Minnesota trial (da Silva *et al.*, 1957). If other currently used vaccine viruses had been subjected to the same type of trial that was conducted at Minnesota similar results might have been obtained.

We do not consider that the small piece of circumstantial evidence we have given above is in any way conclusive proof that wild polioviruses are unstable in their neurotropism, but we do think that these preliminary results might serve as a reminder to those planning attenuated vaccine trials of the sort of problems they have to face in evaluating vaccine safety.

The W.H.O. Expert Committee on Poliomyelitis (World Health Organization, 1958), in its review of present knowledge about live poliovirus vaccines and in its recommendations for trials, virtually ignores the problem of spread. It points out "that preliminary tests on attenuated polioviruses in the hands of several investigators have failed to reveal signs of illness or other harmful effects in the vaccinees *or their associates*" (our italics). Apart from this one oblique reference to spread there is no indication to the reader that it might be important. Whether the committee considered the spread of these vaccine viruses potentially dangerous or not, it was odd that it dismissed the whole problem with such brevity. The uncontrolled spread of poliomyelitis vaccine virus in a community must either be beneficial or potentially dangerous. If spread is dangerous this will be discovered only if field trials are planned with the object of answering this most important question. If spread is beneficial then it would be useful to know this. A new concept in the use of attenuated virus vaccines might be evolved which could be of great value in combating such diseases as influenza, mumps, and measles.

Effectiveness in the Vaccinee

The ultimate test of the effectiveness of attenuated poliovirus vaccines must await controlled field trials if these are in fact possible. In the meantime it seems reasonable to judge likely effectiveness by measuring the levels of neutralizing antibody in vaccinated subjects.

In the trials where virus grown in monkey-kidney-tissue culture has been used the proportion of vaccinees developing neutralizing antibody has usually been over 90%, and the levels of antibody appear to have been satisfactory. With the TN type II rodent-adapted virus we found that a smaller proportion of children developed antibody (77% of 124), but the *levels* of antibody in children who did so were broadly similar to those reported following vaccination with viruses grown in tissue culture. Information about the persistence of neutralizing antibody comes mainly from trials with strains of vaccine virus no longer in use. Our own follow-up study on children vaccinated with TN type II virus (Dane, Dick, Briggs, and Nelson, 1958) is open to this criticism, but we consider that the results obtained with TN type II virus are likely to be at least as good as, or better than, those which will be found with the less virulent current vaccine viruses that do not undergo such a marked change after growth in the human gut. We found that about two months

after vaccination 77% of children had developed neutralizing antibody at levels comparable to that found by others following two injections of formalinized virus (Report, 1957a), and that in a proportion of the children there was a marked decline in antibody level over the next year, which again was like that reported after two injections of formalinized virus (Report, 1957b).

Very high levels of neutralizing antibody have been shown to develop following a third booster injection of formalinized vaccine (Report, 1957b), and it is doubtful whether refeeding with live virus vaccines would have such a marked effect. Furthermore, in view of the alimentary resistance to reinfection which follows vaccination with live virus vaccine, it would be difficult to predict whether or not, or when, reinfection would occur. This does not mean that refeeding would not be a possible way of maintaining immunity induced by live virus vaccines, but only that certain problems would arise which have not arisen with formalinized vaccine.

The alimentary resistance to reinfection which follows vaccination with live virus is often presumed to be some sort of local gut immunity. Little is known about the nature of this immunity or how long it will last, and, although it is of obvious benefit to the individual vaccinee, it may have more far-reaching consequences to the community as a whole.

Effectiveness to the Community

The resistance or comparative resistance of people vaccinated with live attenuated polioviruses to reinfection with these viruses gives hope that they will be similarly resistant to infection with wild polioviruses. If this proves to be the case, then there is a real chance that wild polioviruses might disappear from a community where sufficient numbers had been vaccinated with live virus vaccines. This does not appear to have happened in the U.S.A. following the use of formalinized vaccine, but until a high proportion of the susceptibles in a country have been adequately vaccinated with potent formalinized vaccine the possibility that the elimination of polioviruses from a community can be achieved with this type of vaccine cannot be excluded. Experimentally, Howe (1957) has shown that there was a significant reduction in the amount of virus excreted by chimpanzees fed a virulent strain of poliovirus if they had previously been vaccinated with formalinized virus. Poliovirus infection in chimpanzees is characterized by a greater pharyngeal multiplication than occurs in man, and for this reason a direct comparison may not be valid.

Use and Testing of Current Attenuated Strains

There appear to be four possible uses of attenuated poliovirus vaccines. They could be used (*a*) instead of formalinized vaccines; (*b*) to supplement formalinized vaccines; (*c*) to halt epidemics; and (*d*) in countries whose financial resources do not permit the use of formalinized vaccines.

In the first case, it seems unlikely that any country with the finances available to undertake a vaccination programme using formalinized vaccines would use, or switch to, attenuated virus vaccines until it has been shown that they are as safe as, or safer than, formalinized vaccines and produce as good or better levels of immunity.

In the second case, attenuated virus vaccines might be used to supplement formalinized vaccines in the hope of eliminating wild viruses from the community. Before undertaking such a programme one would like to know whether virulent polioviruses may not in fact be largely eliminated from communities which are efficiently immunized with potent formalinized vaccines. Enough time has not elapsed from the introduction of formalinized vaccines, and sufficiently thorough immunization has not yet been achieved to answer this question.

The use of attenuated vaccines to control epidemics at the present time involves the employment of a contagious virus whose safety and effectiveness during non-epidemic periods has been inadequately studied. It cannot be predicted how avirulent viruses would behave if they were introduced into a community in which conditions are ripe for an epidemic, and in many areas it would be difficult to organize voluntary immunization of a whole population as was done recently in Africa (Courtois *et al.*, 1958). The problems involved in attempting to evaluate the results of vaccinating a community during an epidemic are great enough to deter some authorities from introducing a largely unproved vaccine in this manner.

There remains the possibility that live virus vaccines might be used in countries in which formalinized vaccines cannot be afforded. In our opinion carefully conducted trials of attenuated virus vaccines should be undertaken in such countries if there is a genuine need for vaccination, and they should be done during non-epidemic times of the year. The previous epidemic history of poliomyelitis should be available, and should be carefully considered before initiating the trials. Such trials would be the most valuable first step in gaining information in the field, but it must be appreciated that there are great difficulties in planning trials of a vaccine virus which spreads from vaccinees to their contacts. Any trial of safety must take this factor into account and must attempt to evaluate the harm or good which has been achieved by the uncontrolled spread of a living virus. The information so far published about the currently available attenuated vaccines does not suggest that they will necessarily be either dangerous or completely safe. It is important that trials should aim at defining the limits of safety of these vaccines, rather than at sidestepping the possible dangers which accompany the use of a contagious vaccine.

REFERENCES

Courtois, G., Flack, A., Jervis, G. A., Koprowski, H., and Ninane, G. (1958). *Brit. med. J.*, **2**, 187.

Dane, D. S., Dick, G. W. A., Briggs, Moya, and Nelson, R. (1958). Ibid., **2**, 1187.

—— —— Connolly, J. H., Fisher, O. D., and McKeown, Florence (1957). Ibid., **1**, 59.

Dick, G. W. A., and Dane, D. S. (1957). Ibid., **1**, 70.

—— —— Fisher, O. D., Connolly, J. H., and McKeown, Florence (1957). Ibid., **1**, 65.

Fox, J. P. (1957a). In *Special Publications of the New York Academy of Sciences*, **5**, 152.

—— (1957b). Fourth International Poliomyelitis Conference, Geneva, 1957. In press.

Howe, H. A. (1957). *Amer. J. publ. Hlth.* **47**, 871.

Koprowski, H. (1957). In *Special Publications of the New York Academy of Sciences*, **5**, 128.

—— Norton, T. W., Jervis, G. A., Nelson, T. L., Chadwick, D. L., Nelsen, Doris J., and Meyer, K. F. (1956). *J. Amer. med. Ass.*, **160**, 954.

Langmuir, A. D. (1957). In *Special Publications of the New York Academy of Sciences*, **5**, 93.

Paul, J. R., Horstmann, Dorothy M., Melnick, J. L., Niederman, J. C., and Deutsch, Joyce (1957). In *Special Publications of the New York Academy of Sciences*, **5**, 141.

Report to Committee on Laboratory Investigations of Poliomyelitis, Medical Research Council (1957a). *Brit. med. J.*, **1**, 366.

Report to Medical Research Council (1957b). Ibid., **2**, 1207.

Sabin, A. B. (1957a). In *Special Publications of the New York Academy of Sciences*, **5**, 113.

—— (1957b). Fourth International Poliomyelitis Conference, Geneva, 1957. In press.

da Silva, M. M., McKelvey, J. L., Bauer, H., Prem, K. A., Cooney, Marion K., and Johnson, A. (1957). *Univ. Minn. med. Bull.*, **29**, 133.

Smorodintsev, A. A., Drobishevskaya, A. I., Gorev, N. E., Ilienko, V. I., Kluchareva, T. E., and Kurnosova, L. M. (1958). *Second Scientific Meeting of Institute for Poliomyelitis Research of the Academy of Medical Science. Poliomyelitis and Related Illnesses Caused by Enteric Viruses.* State Publishers for Medical Literature, Moscow.

World Health Organization (1958). *Wld Hlth Org. techn. Rep. Ser.*, No. 145.

"The meat arriving at Smithfield Meat Market has presumably been inspected at the time of slaughter in this country or abroad. Evidence of disease which has escaped notice at the primary inspection is nevertheless found; in some cases it has been overlooked, in others it has only become apparent when the carcass is cut up. Condemnations of meat at Smithfield are to a considerable extent due not to disease but to deterioration during transport, decomposition, bone-taint, brine-staining, etc. The total amount of meat delivered at Smithfield Market was 422,607 tons, of which 497 tons were found to be diseased or unsound and were voluntarily surrendered."—From the *Report of the Medical Officer of Health for the City of London for the Year 1957.*

VACCINATION AGAINST POLIOMYELITIS WITH LIVE VIRUS VACCINES

5. NEUTRALIZING ANTIBODY LEVELS ONE YEAR AFTER VACCINATION

BY

D. S. DANE, B.A., M.B., B.Chir.
Lecturer in Microbiology

G. W. A. DICK, M.D., D.Sc., F.R.C.P.Ed.
Professor of Microbiology

MOYA BRIGGS,* B.Sc.

AND

ROBERT NELSON*

From the Department of Microbiology, The Queen's University, Belfast

During the first half of 1956 small laboratory-studied trials of TN type II and SM type I oral attenuated poliomyelitis vaccines (Koprowski, Norton, Jervis, Nelson, Chadwick, Nelsen, and Meyer, 1956) were made in Northern Ireland (Dane, Dick, Connolly, Fisher, and McKeown, 1957; Dick, Dane, Fisher, Connolly, and McKeown, 1957). Neither of these vaccines fulfilled what we considered to be the necessary theoretical requirements of safety (Dick and Dane, 1957), but the results of investigations into the duration of immunity following their administration are reported here because they may be of some value in predicting the sort of immunity which is likely to follow the use of the more attenuated virus vaccines now available.

Materials and Methods.—The materials and methods used were as described previously (Dane *et al.*, 1957). Comparative results for levels of neutralizing antibody in any individual are given only when paired sera were titrated in the same test.

Results

Persistence of Neutralizing Antibody After Vaccination with SM type I Poliovirus

A number of volunteers who were fed SM type I virus in 1956 were bled at frequent intervals after vaccination in order to estimate the highest titre of antibody which they would develop. The serum with the highest titre from each of six adult volunteers was tested again with another serum taken about a year later. The results of these tests are shown in Table I.

TABLE I.—*Levels of Type I Neutralizing Antibody in Adults at Various Intervals After Vaccination with S.M. Type I Virus*

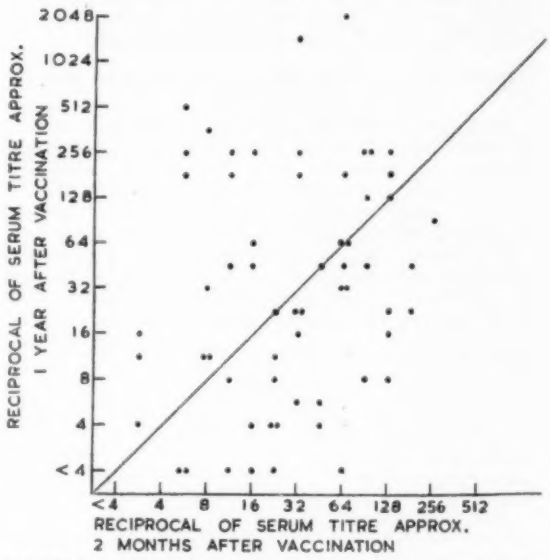
Serial No.	Age	Sex	Pre-vaccination Titre	Weeks After Vaccination	Titre	Weeks After Vaccination	Titre
193	41	M	<4*	7	22	67	<4
218	39	M	<4	6	22	68	11
353	24	F	<4	4	16	68	4
284	20	M	<4	3	179	99	64
212	20	M	<4	5	359	62	89
235	25	M	<4	9	8	72	256

* Reciprocal of serum antibody titre.

The antibody titre had fallen in five of the individuals, but had risen significantly in the other (No. 235). A number of serum specimens taken from No. 235 over the study period were tested in an attempt to explain this rise in antibody. It was found that between the ninth and the fifteenth month after vaccination he had developed a significant rise in neutralizing antibody to both type I (from 1:4 to 1:256) and type II poliovirus (from <1:4 to 1:96). It appears, therefore, that during this time he had had at least one natural poliovirus infection.

Persistence of Neutralizing Antibody After Vaccination with TN type II Poliovirus

Blood samples from 60 children vaccinated orally with TN type II poliovirus in 1956 were taken approximately one year later. The comparative levels of neutralizing antibody in this specimen and one taken about two months after vaccination were estimated by testing the two sera at the same time. The variation in antibody levels during this period is shown in the Chart.



Individual variation of type II neutralizing antibody titre in 60 children following vaccination with TN type II poliovirus. All the children were without type II antibody at the time of vaccination.

In a proportion of the children a significant antibody rise occurred after the first post-vaccination blood specimen had been taken. It is impossible to prove that the antibody rises in these children were not the result of infections with naturally occurring type II polioviruses, but the most satisfactory explanation is that vaccine virus multiplication in the gut (and therefore the antigenic stimulus) continued in these children beyond the date when the first post-vaccination blood sample was taken (approximately the ninth week after vaccination). We have no laboratory data to support this hypothesis, because the trial was originally planned on the basis of observations by Koprowski *et al.* (1956) that TN type II vaccine virus was excreted in scarcely detectable amounts over a short period, and for this reason collection of faecal specimens was not continued long enough. However, a number of children were excreting faecal virus during the fourth week after vaccination, when specimen collection ceased, and there seems to be no reason why they should not have continued doing so for several months, as was the case in children vaccinated with SM type I virus (Koprowski *et al.*, 1956).

The possibility that some of the rises in type II antibody might have been due to natural infections with heterologous poliovirus types was also considered. Serum specimens taken at the time of vaccination and one year later were tested at a 1:4 dilution against types I and III poliovirus to find out whether any children had developed antibody against

*Technicians paid with grants from the National Fund for Poliomyelitis Research and the Medical Research Council.

these poliovirus types. Titrations of the paired sera from children found to have developed antibody showed that six natural infections had occurred—three with type I poliovirus and three with type III poliovirus. In the course of another investigation type I poliovirus had in fact been isolated from two of the children who showed serological evidence of a type I infection.

We conclude that heterotypic poliovirus infections could only have contributed to the late rise in type II antibody in these six instances.

After testing the first post-vaccination blood sample (taken after about two months) we reported that only 77% of 124 children had developed neutralizing antibody following vaccination with TN type II virus (Dane *et al.*, 1957). We were able to obtain blood samples one year later from 15 of the 28 children who did *not* develop antibody. None were found to have developed type II antibody during this interval, thus confirming our original conclusion that the vaccine had failed to "take" in these individuals.

Influence of Heterotypic Antibody on Vaccination with TN Type II Virus

Because of the possibility that previous natural heterotypic poliovirus infections might have influenced the response of children to vaccination with TN type II virus, pre-vaccination samples of blood from 110 children who had been vaccinated with TN type II virus were tested for neutralizing antibody at a 1:4 dilution against types I and III poliovirus. The pre-vaccination antibody patterns found are shown in Table II. Children possessing different pre-vaccination heterotypic antibody patterns showed no significant difference in their response to vaccination.

TABLE II.—*Poliomyelitis Neutralizing Antibody Patterns at the Time of Vaccination in* 110 *Children Fed TN Type II Virus in* 1956

No. of Children	Type I Antibody	Type II Antibody	Type III Antibody
63	—	—	—
20	+	—	—
19	—	—	+
8	+	—	+

— = Titre of < 1 in 4. + = Titre of > 1 in 4.

Discussion and Conclusions

The neutralizing antibody levels which we found in children one year after vaccination with TN type II virus were of the same order as those reported in non-immune children who had received two injections of formalinized vaccine a year before (Report, 1957). A number of the TN-vaccinated children were found to have had a marked decline in their neutralizing antibody level over the year, and our previous finding that 23% of children failed to develop antibody after vaccination was confirmed.

One of the advantages claimed for oral attenuated poliomyelitis vaccines is that they will produce a more durable immunity than formalinized vaccines. We can find no evidence that this was true in a proportion of children vaccinated with TN type II virus. Admittedly our yardstick for the measurement of immunity has been circulating neutralizing antibody. Some sort of local gut immunity follows infection with oral poliovirus vaccines, but in the absence of more precise information about this local immunity it would be unwise to assume that it is more durable than circulating antibody.

Further trials of Koprowski's TN type II vaccine have been abandoned because the virus is liable to change its character and become virulent after growth in the human gut. If it can be shown that the recently developed more highly attenuated poliovirus vaccines do not suffer from this drawback, then it would seem desirable to show also that they can produce a reasonably durable immunity in the majority of vaccinated subjects before they are used on a large scale. On the basis of the results reported here we do not think that durability of immunity should be considered as an automatic benefit associated with living vaccines.

We wish to acknowledge grants from the National Fund for Poliomyelitis Research, the Medical Research Council, and the Northern Ireland Hospitals Authority.

REFERENCES

Dane, D. S., Dick, G. W. A., Connolly, J. H., Fisher, O. D., and McKeown, Florence (1957). *Brit. med. J.*, **1**, 59.
Dick, G. W. A., and Dane, D. S. (1957). Ibid., **1**, 70.
—— —— Fisher, O. D., Connolly, J. H., and McKeown, Florence (1957). Ibid., **1**, 65.
Koprowski, H., Norton, T. W., Jervis, G. A., Nelson, T. L., Chadwick, D. L., Nelsen, Doris, J., and Meyer, K. F. (1956). *J. Amer. med. Ass.*, **160**, 954.
Report to Committee on Laboratory Investigations of Poliomyelitis, Medical Research Council (1957). *Brit. med. J.*, **1**, 366.

A SMALL-SCALE TRIAL OF TYPE III ATTENUATED LIVING POLIOVIRUS VACCINE

BY

SUZANNE K. R. CLARKE, M.D.
Lecturer in Bacteriology, University of Bristol; formerly Lecturer in Bacteriology and Virus Diseases, University of Sheffield

A. P. GOFFE, M.B., B.S., Dip.Bact.

C. H. STUART-HARRIS,* M.D., F.R.C.P.
Professor of Medicine, University of Sheffield

AND

E. G. HERZOG, M.B., B.S.
Surgeon Superintendent, King Edward VII Orthopaedic Hospital, Sheffield

From the Virus Research Laboratory, University of Sheffield, and the Wellcome Research Laboratories, Beckenham, Kent

The purpose of this small-scale trial of a single strain of living attenuated poliovirus vaccine was to obtain information concerning the capacity of the virus to induce infection in children previously immunized with inactivated Salk-type vaccine, to measure the antibody formation after the feeding of the virus, and to compare the virulence for monkeys of excreted virus with that of the strain composing the vaccine. In addition, evidence was sought concerning the spread of virus from vaccinated children to their contacts. The virus vaccine selected for use was the type III attenuated poliovirus from culture of monkey-kidney tissue developed by Dr. Albert B. Sabin and obtained as virus-containing culture fluid from Dr. J. D. Verlinde at Leyden. The virus was the highly purified Leon strain previously subjected to many kidney-tissue-culture passages and plaque-selection, and designated the $12a_1b$ (KP4) virus (Sabin, 1957). The strain pool was freshly titrated by one of us (A. P. G.) upon receipt and found to have a titre of $10^{7.33}$ 50% tissue-culture infective doses per ml.

Control Period of Study

The test was carried out in a long-stay orthopaedic institution where the children were under treatment for lesions such as those due to Perthes's disease or tuberculous arthritis. A control period of study began in September, 1957, when immunization with two doses of British-type Salk vaccine was given to certain boys whose parents volunteered for their inoculation. Nineteen boys aged 6 to 15 years received vaccine intramuscularly after a preliminary withdrawal of 10 ml. of blood. The second dose of vaccine was given one month after the first dose, and all inoculations were completed by December 4, 1957. A second specimen of blood was obtained two weeks after the second

*In receipt of a grant from the Medical Research Council and the National Fund for Poliomyelitis Research.

dose of vaccine, and the neutralizing antibody contents of the pre- and post-immunization sera were estimated by titration in monkey-kidney-tissue cultures against each of the three types of poliovirus (Tyrrell *et al.*, 1956).

Permission to use live poliovirus as a boosting vaccine was sought from the parents of those who had received Salk-type vaccine and was given in 14 instances. The children were housed in two wards prior to the trial. One of these contained 12 children aged 6 to 8, of whom five eventually went into the trial, while the remaining nine children in the trial came from a second ward of 12 children aged 9 to 15. Faeces were obtained once weekly for 17 weeks from all children in the first ward and for a further three weeks from all children who were to receive live virus in both wards. In no instance was a strain of poliovirus obtained from the faecal suspensions tested in pools of three to four specimens which were inoculated into monkey-kidney-tissue cultures. This preliminary period of testing was considered desirable because patients convalescent from poliomyelitis were nursed in the same hospital. But their wards were in a separate building situated at least 200 yards (180 m.) from the main block of the hospital. Segregation of the patients in the respective sections was complete. The only natural virus strains recovered in Sheffield at any time from September, 1957, to April, 1958, had been obtained by Dr. J. E. M. Whitehead at the Public Health Laboratory, Sheffield, during the acute phase of illness prior to the transfer of patients with poliomyelitis to the orthopaedic hospital. All were of type I poliovirus. No case of type III poliomyelitis was in fact encountered in Sheffield during the entire period of the trial, and the last case of type III virus isolation had been in December, 1956.

Period of the Trial

The 14 boys aged 6 to 15 years who were to receive live virus vaccine were collected together and were the sole inmates of one ward on February 16, 1958. They were attended by nurses who had been previously immunized with two doses of Salk-type vaccine. All but three of the boys were confined to bed, and some were immobilized on frames during the period of observation.

Virus was fed orally in hard gelatin capsules containing a dilution of stock vaccine virus in sterile synthetic medium 199 mixed with polyethylene glycol 400 so as to contain $10^{4.5}$ TCD_{50} infective doses of virus in a volume of 0.2 ml. A third sample of blood was obtained from each boy prior to virus feeding, which was carried out in two stages.

On February 17 seven boys received capsules containing virus and seven received capsules filled with uninfected culture medium. Faecal specimens were obtained daily or when passed from all the boys during the ensuing weeks, and occasional specimens were obtained from the nurses in contact with the boys.

The second stage of the feeding of virus took place on March 10, 1958, when 11 boys, including all those previously fed dummy capsules, received a capsule containing live virus similar in amount to that previously used. Faecal specimens continued to be obtained at frequent intervals from all children found to be excreting virus, until the specimens were negative. A fourth sample of serum was collected from all the boys on April 1, six weeks after the first virus feeding and three weeks after the second administration of virus. These serum samples, together with the third samples, were titrated for neutralizing antibodies to the three types of poliovirus as before. The results obtained with these sera and also with the faecal specimens are described after details have been given of the technical methods which were used.

Technical Methods: (a) Sheffield

Isolation of Poliovirus from Faeces

Faeces were stored at −25° C. until tested. Emulsions of 10–30% were then made in Hanks's saline, which contained 1,000 units of penicillin and 1,000 units of streptomycin per ml. Each emulsion was centrifuged at 3,000 r.p.m. for one hour, and 0.5 ml. of the supernatant was inoculated into each of four monkey-kidney-tissue culture tubes containing 1.5 ml. of medium. Trypsinized monkey-kidney-tissue cultures were prepared as described by Balducci *et al.* (1956) from rhesus and cynomolgus monkeys. The maintenance medium consisted of 2% calf serum and 0.25% lactalbumin hydrolysate in Hanks's saline to which three times the normal amount of 1.4% $NaHCO_3$ solution had been added. Three to six hours after inoculation the emulsion was removed from the cultures and fresh medium added. When specific cytopathogenic changes appeared the medium and cells were harvested and stored at −25° C. If no cytopathogenic change appeared after 12 days' incubation the cultures were harvested and a second blind pass was made. This was also incubated for 12 days, and if any suspicious cytopathogenic effect appeared a third pass was made. The faeces collected during the control period were tested in pools of three or four specimens, and only one pass in monkey-kidney-tissue culture was made unless suspicious cytopathogenic effects appeared. Throughout the period of the trial, when faeces were collected and examined no live poliovirus of any type was used in the Sheffield laboratory and no faeces from other sources were examined. The neutralization tests on the serum specimens were done before and after this period.

Titration of Faeces

Accurate 10% emulsions were made from most of the virus-containing faeces. Tenfold dilutions of these emulsions were made in Hanks's saline, and 0.2 ml. of each dilution was inoculated into each of two monkey-kidney-tissue culture tubes containing the medium as used for isolation. End-points were calculated by the method of Reed and Muench (1938).

Neutralization Tests

Sera previously stored at −25° C. were inactivated at 56° C. for 30 minutes and serial fourfold dilutions made in Hanks's saline. The same pools of virus were used in each batch of tests. They were diluted in Hanks's saline, so that 50 TCD_{50} were inoculated into each of the tissue-culture tubes. Equal volumes of serum dilution and virus dilution were mixed in screw-capped bottles and allowed to stand at room temperature for one hour. Into each of two monkey-kidney-tissue culture tubes 0.5 ml. of each mixture was then inoculated. The tests were read daily and the end-points calculated for the day after full degeneration had occurred in the control tubes (usually the fifth day after inoculation). The titres were expressed as the reciprocals of the serum dilutions before the addition of virus. The titre was estimated as "2" when the end-point was less than 4 on the final day of reading the test but where some antibody had been detected at readings on earlier days. The titre was expressed as "less than 4" if no neutralization was apparent when a cytopathogenic effect first appeared in the control tubes. However, the technique was not sensitive enough for detection of very small amounts of antibody. The specimens taken before and after Salk vaccination or before and after feeding the live vaccine for each child were tested at the same time. A control serum was included in each batch of tests.

Technical Methods: (b) Beckenham

Virus Titrations

Each virus pool inoculated into monkeys was titrated for tissue-culture infectivity. Trypsinized rhesus or cynomolgus monkey-kidney cultures in roller tubes were used when an abundant healthy monolayer of epithelial cells was present. Cultures were maintained on a protein-free medium devoid of inhibitors which had been shown to be of optimum sensitivity for demonstrating the cytopathic effect of poliovirus; it consisted of 5% horse-liver digest ultrafiltrate in Earle's balanced salt solution (S. E. Smith, personal communication, 1958). Serial tenfold dilutions up to 10^{-9} of each virus were made in this medium, and 0.5 ml. of each dilution was inoculated into 10 cultures each containing

1.5 ml. of freshly changed medium. Cultures were examined up to the seventh day after inoculation, when final readings were taken and the 50% tissue-culture degeneration end-point (TCD_{50}) was calculated by the method of Kaerber (Irwin and Cheeseman, 1939). Each pool selected for virulence study was titrated on the day it was inoculated into monkeys, and again on a subsequent date together with all other virus pools using one tissue-culture batch. Differences between the two titrations varied between zero and 0.5 log_{10}. In Table III the quantities of virus are expressed as TCD_{50} per ml. of culture fluid and are derived from the mean of the titrations.

The vaccine virus has been titrated four times. It was received frozen at −70° C. and was thawed and titrated; smaller lots were distributed into ampoules and refrozen at −70° C. Three ampoules have been thawed for titration subsequently. The first titration gave a value of 7.55 log TCD_{50} per ml. Three titrations of the refrozen material gave values of 6.7, 6.8, and 6.9 log TCD_{50} per ml., indicating a fivefold loss by this procedure. Since twice-thawed material was used for both feeding and virulence tests the value of $10^{6.8}$ TCD_{50} per ml. has been used.

Virulence Tests

A test for virulence, semi-quantitative in nature, was done on the vaccine, as fed to the children, and on two samples of excreted virus from each child proved to be a virus carrier. The first and the last virus strains isolated from the faeces during the study period were tested, except in one child where the virus excreted on the second day after feeding was tested because the first-day specimen contained very little virus. Tissue-culture fluids of the first passage from cultures inoculated with faecal suspensions were pooled when a full cytopathic effect was apparent, and these fluids were used for the virulence experiment.

Each virus pool was inoculated undiluted into two or three monkeys and diluted 1 in 100 into two or three monkeys. Normal cynomolgus monkeys, between 1.2 and 2.9 kg. in weight, received 1 ml. of sample intracerebrally under thialbarbitone, 0.5 ml. being placed in each thalamic region (Bodian, Morgan, and Schwerdt, 1950). Monkeys were observed for up to 30 days after inoculation, during which time they were isolated in groups of two or three in cages measuring 3 ft. (90 cm.) high by 2 ft. (60 cm.) square, and were not removed unless obviously paralysed. It became apparent during the experiment that this method of observation had a high threshold; minor grades of paralysis were almost certainly missed through not exercising monkeys in an open run. Monkeys showing severe paralysis were sacrificed immediately; those showing minor paralysis were watched over for one or two days for further spread; one monkey showing only moderate involvement of both legs on the 14th day was kept until the 29th day with a fair degree of recovery. All surviving monkeys were killed between the 28th and 30th days after inoculation. At post-mortem examination, samples of blood and lumbar enlargement of spinal cord were taken for recovery of virus, after which the whole animal was fixed by perfusion with 10% formol-saline. Selected lengths of lumbar, thoracic, and cervical cord were processed for histological examination.

Results of the Trial

Clinical

No clinical reactions which could be related to the administration of the live vaccine were detected in the boys or in their contacts. Virus excretion which was believed to signify actual infection therefore occurred in the absence of those clinical phenomena, such as pyrexia, minor illness, and so on, which may accompany the non-paralytic form of clinical poliomyelitis.

Virus Excretion

Excretion of the virus was detected in 6 of the 14 subjects who received live virus by mouth, and in five cases was prolonged and quantitatively considerable in amount. Virus strains were recovered from 2 of the first 7 boys fed virus and from 4 of the 11 fed virus on the second occasion. Four who were fed virus on two occasions and who did not excrete virus on the first occasion also failed to excrete virus on the second occasion. Nor were viruses recovered from the seven boys given dummy capsules during the first stage of the trial, when two other boys were actively excreting virus, or from nurses at any phase of the trial. No evidence of spread of virus to contacts was thus obtained, but it happened that all the boys who excreted virus were immobilized on Jones frames during the entire period of the trial.

The amounts of virus detected in the stools of five of the six boys who excreted virus are shown in Table I. The

TABLE I.—*Amount of Virus in Faeces ($Log_{10}TCD_{50}/G.$) from Five Children who Excreted Virus*

Day After Feeding	Case No.				
	1202	1203	1201	1205	1308
1	1·1				1·1
2	4·2	+	–	3·0	
3	4·7				
4			–		4·7
5	4·2	5·0			
6	5·2				3·2
7	5·2		2·2	2·2	
8	4·2	1·7			
9					3·2
10	5·2		+		–
11	3·7				–
12		2·7	+	1·7	
13	3·2	3·2			
14	2·2	2·2			
15	–			1·7	
16					
17	–		2·2		–
18		–			
19					
20	–	–		+	
21			3·0		
22	–				
23			+		
24					
25					
26					
27		–			
28	–				
29					
30					
31		–	+	1·3	
32					
33					
34	–				
35					
36					
37					
38			–	–	

– = No poliovirus isolated.
+ = Poliovirus isolated but insufficient specimen for titration.

sixth boy (1311) excreted a very small amount of virus for only 24 hours after oral feeding. As this virus was detected only after three tissue-culture passes it seems likely that it represented vaccine virus which had passed through but did not multiply in the intestinal tract. The five boys shown in Table I excreted quantities of virus varying from 1.1 to 5.2 log_{10} 50% tissue-culture infective doses of virus per gramme of stools. Excretion occurred for periods from 9 up to 30 days including the day on which virus was first detected. It is certain that multiplication of virus had taken place in the alimentary tract of these five children. The viruses recovered from each of two specimens of faeces from each child were typed by neutralization techniques. All were found to belong to type III poliovirus.

Antibody Response

The results of serum neutralization tests on all 14 of the boys in whom the trial was made are shown in Table II. The rise in antibodies after the two doses of Salk-type vaccine were of the same order as those found by other workers (M.R.C. Committee, 1957; Russell, 1958). Good antibody responses were obtained in most of the boys, but one boy (1203) failed to respond to the type III antigen and one (1200) to the type I antigen. After the feeding of the live vaccine children who did not excrete virus and the

one boy with transient excretion showed no increase or a twofold decrease in antibody to type III virus and variations with a twofold increase or decrease in antibodies to the other types. Of the five children who excreted virus for prolonged periods one showed no change in antibody levels and one showed a twofold decrease in antibody to type III virus. The remaining three children all showed a fourfold or greater increase in type III antibody without any significant alteration in antibodies to the other poliovirus types. The two children who showed no antibody response after the live virus vaccine had received the second dose of inactivated vaccine 2½ and 4½ months previously. This relatively short interval of time may have been responsible for their failure to develop a further increase in antibody.

In such a small number of subjects it is clearly impossible to discern correlations between the ability of the oral vaccine to establish infection and the antibodies pre-existing in the blood. Of the five who became infected, two had no antibody to type III virus before the administration of Salk-type vaccine, and only one of those who failed to become infected was similarly devoid of such antibody. On the other hand, the geometric mean titre of the type III antibodies just prior to feeding was 42.2 in those who developed infection compared with a mean titre of 351.8 in those who proved resistant to infection. Finally, four of the five boys who became infected were among the youngest subjects in the trial, so that it is possible that age is as important a factor in determining the likelihood of infection as is naturally or artificially acquired antibody.

Neurotropism of Excreted Viruses

The comparative virulence for monkeys of the vaccine virus and of the strains of virus excreted by the five boys considered to have developed an alimentary infection is shown in Table III.

None of the monkeys inoculated with vaccine showed either paralysis or other evidence of neurotropic activity. On the other hand, each child in whom the vaccine virus multiplied excreted at some stage a virus of increased virulence. The viruses included in Table III show a graded spectrum of neurotropic activity which bore a distinct relationship to the length of time that the virus had had to multiply after the original feeding. Thus Case 1308 on the first day and Case 1205 on the second day showed viruses of similar behaviour to the vaccine. Cases 1203 and 1202 on the second day showed some slight increase in paralytic activity. Every strain after the second day showed paralytic activity at the lower concentration of virus inoculated. With the exception of Case 1201, in whom the 7th-day and 31st-day virus both showed strains of intermediate virulence, all cases showed an increased virulence in the strain of virus excreted later compared with that excreted in the earlier phase of infection. On the 14th day Case 1203 showed a degree of neurotropism similar to that of field strains of type III virus from paralytic cases. Eight thousand tissue-culture doses given intracerebrally caused severe paralysis of relatively rapid onset in two monkeys and extensive histological lesions in a third monkey. One monkey had viraemia at the onset of paralysis on the sixth day after receiving the lower dilution of virus.

TABLE III.—*Intracerebral Virulence Test in Monkeys*

Case No.	Days after Feeding	Virus Titration*	Estimated TCD_{50} Inoculated	Paralytic Rate	Day of Onset Paralysis	Histological Infection Rate	Virus Recovery from Cord
Vaccine (diluted and refrozen)	—	6·8	6,400,000	0/3	—	0/3	0/3
			64,000	0/3	—	0/3	0/3
1201	7	7·95	89,000,000	1/3	15	3/3	1/3
			890,000	2/3	6, 22	2/3	2/3
1201	31	8·15	140,000,000	2/2	4, 9	2/2	2/2
			1,400,000	1/3	16	3/3	2/3
1202	2	7·65	45,000,000	2/2	9, 9	2/2	2/2
			450,000	0/3	—	2/3	1/3
1202	14	6·85	7,000,000	1/3	8	3/3	1/3
			70,000	1/3	29	3/3	2/3
1203	2	7·1	12,000,000	1/3	19	1/3	1/3
			120,000	0/3	—	0/3	0/3
1203	14	5·9	800,000	3/3	6, 7, 8	3/3	3/3†
			8,000	2/3	8, 10	3/3	2/3
1205	2	6·8	6,400,000	0/2	—	0/2	0/2
			64,000	0/3	—	0/3	0/3
1205	31	6·9	8,000,000	1/3	16	3/3	0/3
			80,000	1/3	28	1/3	1/3
1308	1	7·2	16,000,000	0/3	—	0/3	0/3
			160,000	0/3	—	0/3	0/3
1308	9	6·95	8,900,000	2/2	7, 16	2/2	1/2
			89,000	1/2	15	1/2	0/2

* Mean of two titrations. $Log_{10}TCD_{50}$ ml.
† Monkey paralysed on sixth day also showed viraemia.

As will be noted from Table III, the extent of involvement of the spinal cord revealed by histological examinations was greater than that shown by clinical assessment of the monkeys from outside their cages. The lesions in some cases were indeed extensive and severe, as can be seen from Figs. 1, 2, and 3. All the viruses recovered from the spinal cords of these monkeys were type III. No other strain of poliovirus was being used in the unit housing the monkeys during the period of these experiments.

Discussion

The use of living attenuated viruses for immunization against poliomyelitis is now being actively pursued by several different groups of observers. There are, however, few recorded observations concerning the use of such vaccine as an agent for reinforcing the basic immunity acquired by immunization with Salk vaccine. Paul *et al.* (1957) reviewed the argument for such a use of an attenuated live virus vaccine and suggested that it might be desirable to obtain a planned exposure to an attenuated virus by mouth rather than to rely upon natural infection with an unpredict-

TABLE II.—*Neutralizing Antibody Titres in* 14 *Children*

Case No.	Age	Type III Virus				Type I Virus				Type II Virus			
		1	2	3	4	1	2	3	4	1	2	3	4
(a) Children who excreted virus after feeding type III virus vaccine													
1201	7	<4	256	128	128	32	512	128	128	512	2,048	2,048	2,048
1202	6	16	64	64	256	128	512	512	512	8	512	512	512
1203	6	4	4	8	512	512	2,048	4,096	4,096	<4	128	64	128
1205	6	<4	32	8	2,048	<4	8	2	<4	2	128	16	32
1308	10	8	256	256	128	32	512	1,024	512	<4	128	128	64
(b) Children who did not excrete virus after feeding vaccine													
*1200	6	32	1,024	512	512	2	2	<4	<4	<16	64	8	16
1203	15	<4	8	16	16	<4	64	64	128	>4	4,096	8,192	4,096
1304	15	32	512	2,048	2,048	8	1,024	512	1,024	<16	256	128	64
*1305	12	16	2,048	2,048	1,024	512	1,024	256	512	128	1,024	256	512
1306	10	4	1,024	4,096	2,048	128	512	256	256	16	1,024	512	256
*1307	14	8	256	512	512	8	64	128	128	128	512	2,048	1,024
*1310	11	2	8	8	8	<16	512	512	512	128	2,048	2,048	2,048
1312	9	128	512	512	256	32	1,024	1,024	512	<4	128	128	128
(c) Transient excretion virus after feeding vaccine													
1311	9	2	2,048	1,024	1,024	<4	8	8	8	8	1,024	2,048	2,048

1 = Before Salk-type vaccine. 2 = After Salk-type vaccine. 3 = Before feeding type III virus vaccine. 4 = After feeding type III virus vaccine.
* Fed virus on two occasions.

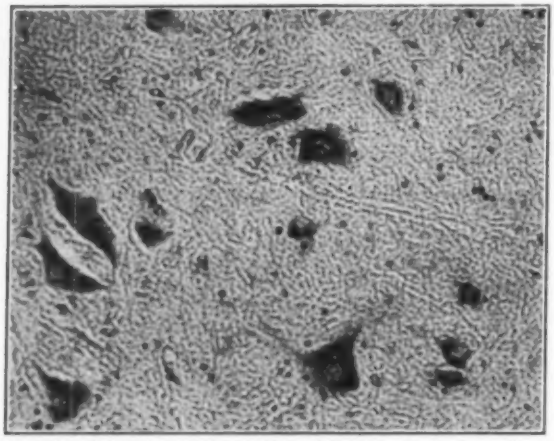


FIG. 1.—Photomicrograph (×170) of lumbar cord of monkey killed 28 days after intracerebral inoculation of $10^{6.5}$TCD$_{50}$ of vaccine virus. No paralysis, normal histological appearance. Nissl stain.

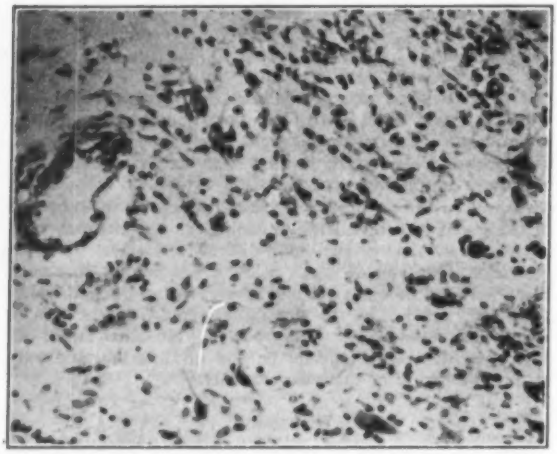


FIG. 2.—Lumbar cord of monkey paralysed eight days after intracerebral inoculation of $10^{5.5}$TCD$_{50}$ of virus from faeces of Case 1203 on the 14th day after vaccine. Typical lesions of acute poliomyelitis. Type III virus isolated.

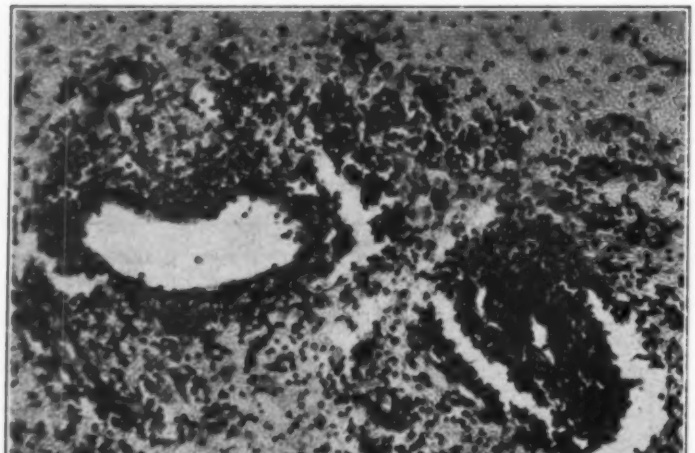


FIG. 3.—Lumbar cord of monkey killed 29 days after intracerebral inoculation of $10^{6.0}$TCD$_{50}$ of virus from faeces of Case 1202 on the 14th day after vaccine. Extensive lesions typical of convalescent poliomyelitis. Type III virus isolated.

able dose of wild possibly virulent poliovirus. They showed (Horstmann *et al.*, 1957b) that a child of 9 vaccinated previously with Salk vaccine was readily infected by live attenuated type III virus (Leon—KP34) fed by mouth. In a later trial of type I virus (L.Sc. strain) under conditions where spread of infection readily occurred to contacts, Horstmann *et al.* (1957a) found that children immunized with Salk vaccine acquired alimentary infection in 10 out of 10 instances after virus-feeding by mouth and in 12 out of 13 instances by natural exposure. These observations are paralleled by the occurrence of alimentary infection under natural circumstances in previously vaccinated children who were family contacts of cases of poliomyelitis (Lipson *et al.*, 1956; Gelfand *et al.*, 1957; Davis *et al.*, 1958). It thus appears likely that children who have received Salk-type of inactivated poliomyelitis vaccine can readily become infected under natural conditions or after deliberate feeding of poliomyelitis virus. Yet the observations of Sabin (1956) and of Horstmann *et al.* (1957a) showed that persons whose blood contained naturally acquired antibodies frequently resisted infection by live attenuated viruses fed by mouth, thus suggesting that the alimentary tract does acquire immunity after exposure to poliovirus.

Our own study has confirmed the fact that it is possible to infect the alimentary tract of children previously immunized with two doses of Salk-type vaccine in spite of the presence of antibodies in the serum at the time of infection. Too few of the children lacked type III antibody prior to immunization with Salk-type vaccine for us to throw any light on the relative protective power of natural versus artificially acquired antibody, though the data suggested that age of the subject may be a factor in this question of immunity. The circumstances of our trial were also too restrictive for the observation that spread of virus did not take place from carriers to contacts to have much significance. No spread of infection was in fact observed by Horstmann *et al.* (1957b) in the study of a similar attenuated type III virus in a ward of 13 mentally defective children and adults. On the other hand, the L.Sc. type I attenuated virus fed in the later study of Horstmann *et al.* (1957a) to mentally retarded children spread widely, so that strain differences as well as the circumstances of the trial may be important in determining whether or not contact infection will occur.

The antibody-boosting capacity of infection with attenuated poliovirus proved less uniform than was expected. One explanation of the failure of two of the five infected children to react may be that the recent boost of antibody consequent upon the injection of Salk-type vaccine had interfered with the capacity of the alimentary infection to raise the antibodies to a still higher level (Sabin, 1957). However, Dick and Dane (1957), who worked with the rodent-adapted type II strain developed by Koprowski *et al.* (1956), similarly recorded a failure of uniformity in antibody response after oral feeding.

Probably the most important of our observations are those relating to the comparative virulence of the vaccine virus which was fed and that of the strains of virus recovered from the stool. Tests on the vaccine virus fully confirmed Sabin's opinion concerning the high degree of attenuation of this virus for the brain and spinal cord of the monkey. However, all the children whose faeces contained virus for several days after oral feeding excreted strains with a capacity to induce paralysis in monkeys inoculated intracerebrally. Sabin (1957) found that the viruses excreted by persons fed attenuated poliovirus strains had an altered neurotropism in that they would sometimes produce paralysis after direct intraspinal inoculation into monkeys. Some increase in intracerebral activity was also

recorded, more frequently for type III than for types I and II, but less consistently and of a lower order than that recorded above. However, the majority of viruses examined by Sabin were isolated early in excretion; in common with our finding, increased neurotropism was found most often at a later stage of excretion. Nevertheless, Sabin considered that such excreted viruses were less highly neurotropic than wild polioviruses disseminated by healthy children during non-epidemic periods.

It is a matter of opinion whether all the viruses excreted by the children in our trial were less virulent than strains encountered in nature. But the degree of alteration from the original vaccine strain appeared to be considerable. In this regard our observations seem to be similar to those recorded by Dane *et al.* (1957) with rodent-adapted type II virus and by Dick *et al.* (1957) with modified type I virus (Koprowski *et al.*, 1956). It will be recalled that Dick and Dane (1957) stated that these virus strains were unacceptable for mass immunization because of their alteration in virulence during passage through the alimentary tract. In spite of the mass use of living attenuated poliovirus vaccine in the Belgian Congo (Courtois *et al.*, 1958) it is our opinion that further research concerning the properties of the viruses excreted by those receiving such vaccines is desirable in order to reconcile the conflicting evidence.

Summary

Fourteen children who were patients at a long-stay orthopaedic hospital were immunized with two doses of British inactivated poliovirus vaccine and were later given living attenuated type III virus vaccine (Sabin) by mouth in gelatin capsules. No adverse clinical reactions were observed. Five of the children developed an alimentary infection, as shown by excretion of virus in the stools for from 9 to 30 days, and in three instances by a further increase in antibody titre. No instance of spread of excreted virus to contacts was detected. The vaccine virus and some of the viruses excreted early in the course of infection did not produce paralytic effects in monkeys inoculated intracerebrally. All five infected children excreted strains of virus possessing enhanced neurotropic properties for monkeys at a late stage of the infective process.

We wish to thank Dr. A. B. Sabin for kindly permitting us to use the attenuated type III virus vaccine. Dr. V. Udall, of the Wellcome Research Laboratories, gave much assistance in the histological examination of the monkey nervous tissue.

References

Balducci, D., Zaiman, E., and Tyrrell, D. A. J. (1956). *Brit. J. exp. Path.*, **37**, 205.

Bodian, D., Morgan, I. M., and Schwerdt, C. E. (1950). *Amer. J. Hyg.*, **51**, 126.

Courtois, G., Flack, A., Jervis, G. A., Koprowski, H., and Ninane, G. (1958). *Brit. med. J.*, **2**, 187.

Dane, D. S., Dick, G. W. A., Connolly, J. H., Fisher, O. D., and McKeown, F. (1957). *Brit. med. J.*, **1**, 59.

Davis, D. C., Lipson, M. J., Carver, D. H., Melnick, J. L., and Robbins, F. C. (1958). *Pediatrics*, **22**, 33.

Dick, G. W. A., and Dane, D. S. (1957). *Brit. med. J.*, **1**, 70.

—— —— Fisher, O. D., Connolly, J. H., and McKeown, F. (1957). Ibid., **1**, 65.

Gelfand, H. M., Fox, J. P., and LeBlanc, D. R. (1957). *Amer. J. publ. Hlth.*, **47**, 421.

Horstmann, D. M., Niederman, J. C., Melnick, J. L., and Paul, J. R. (1957a). *Trans. Ass. Amer. Phys.*, **70**, 91.

—— Paul, J. R., Melnick, J. L., and Deutsch, J. V. (1957b). *J. exp. Med.*, **106**, 159.

Irwin, J. O., and Cheeseman, E. A. (1939). *J. Hyg. (Camb.)*, **39**, 374.

Koprowski, H., Norton, T. W., Jervis, G. A., Nelson, T. L., Chadwick, D. L., Nelsen, D. J., and Meyer, K. F. (1956). *J. Amer. med. Ass.*, **160**, 954.

Lipson, M. J., Robbins, F. C., and Woods, W. A. (1956). *J. clin. Invest.*, **35**, 722.

Medical Research Council (1957). *Brit. med. J.*, **1**, 366.

Paul, J. R., Horstmann, D. M., Melnick, J. L., Niederman, J., and Deutsch, J. (1957). *N.Y. Acad. Sci.* Spec. Monograph, **5**, 141.

Reed, L. J., and Muench, H. (1938). *Amer. J. Hyg.*, **27**, 493.

Russell, K. (1958). *Brit. med. J.*, **1**, 622.

Sabin, A. B. (1956). *J. Amer. med. Ass.*, **162**, 1589.

—— (1957). Ibid., **164**, 1216.

Tyrrell, D., Keeble, S. A., and Wood, W. (1956). *Brit. med. J.*, **1**, 598.

COMBINED GASTRIC AND DUODENAL ULCERATION

A SURVEY OF 157 CASES

BY

R. MANGOLD, M.D.

From the Department of Gastro-enterology, Central Middlesex Hospital, London

From the time Sir David Wilkie (1926) first reported on combined ulceration of the stomach and duodenum there has been a considerable divergence of opinion in respect to its incidence. This is revealed in the recent observations by Feldman (1953) and by Johnson (1955). From their papers it would appear that surgeons as a rule observe a much higher proportion than is found in either post-mortem or radiological studies. Johnson also drew attention to gastric retention as leading to gastric lesions in patients suffering from chronic duodenal ulcer. The present study shows the incidence of combined ulcers as encountered in a general hospital, and gives some additional information on duodenopyloric stenosis causing secondary ulcer of the stomach. It also reveals the increased danger of bleeding, making surgical treatment more advisable than with a single ulcer.

Material

The 157 cases reported here were collected from the files of the in-patient and out-patient clinics of the Central Middlesex Hospital, London. Only cases with combined ulcers first diagnosed in the years 1947 to 1954 were included. Definite radiological, surgical, or post-mortem evidence of chronic ulceration was required. Acute ulcers were excluded. In all doubtful cases the *x*-ray films were reviewed. While the work proceeded, it became increasingly obvious that cases with antral, prepyloric, and pyloric ulcers were not suitable for analysis. There would often arise considerable doubt about the exact location of the ulcer. Extensive scarring due to prepyloric lesions will sometimes lead to secondary duodenal deformity, particularly after perforation. For this reason, only gastric ulcers at or above the angulus were included.

Incidence

During the eight-year period from 1947 to 1954, 157 cases showing both gastric and duodenal ulcers or ulcer scars were observed. In 139 of these, both ulcers were diagnosed radiologically. During the same period 3,744 duodenal and 1,352 gastric ulcers were detected by *x*-ray study in the hospital, excluding the combined lesions. Based on *x*-ray findings, the observed incidence is 2.7%. As mentioned above, cases with prepyloric ulcers were not included in the combined ulcer group. Ihre and Müller (1943) observed 26% of all benign gastric ulcers to be prepyloric. Many authors give figures lying between 15 and 20%, but Gott,

TABLE I.—*Incidence of Combined Ulcers Based on X-ray Investigation (Central Middlesex Hospital, 1947–54)*

No. of Cases With Single Ulcers	Combined Ulcers (Prepyloric Ulcers Excluded)		Combined Ulcers (Estimated 25% Prepyloric Ulcers Included)	
	No.	Incidence	No.	Incidence
D.U. .. 3,744	139	$\frac{139\times100}{3,744+139}=3{\cdot}6\%$	185	$\frac{185\times100}{3,744+185}=4{\cdot}7\%$
G.U. .. 1,352*	139	$\frac{139\times100}{1,352+139}=9{\cdot}3\%$	185	$\frac{185\times100}{1,352+185}=12{\cdot}0\%$
All ulcers 5,096	139	$\frac{139\times100}{5,096+139}=2{\cdot}7$	185	$\frac{185\times100}{5,096+185}=3{\cdot}5$

* Including prepyloric ulcers.

Shapiro, and Kelty (1954) found 42% of gastric ulcers below the angulus. If an estimated 25% of prepyloric ulcers are added, the number of combined ulcers would increase to 185 and the incidence to 3.5% (Table I). Thus one in every eight hospital patients suffering from an ulcer of the stomach and about 1 in 30 patients having a duodenal ulcer or ulcer scar may be expected to have an associated ulcer of the other organ as well.

It has been suggested by Johnson (1955) that many combined ulcers may be missed on *x*-ray examination, thus decreasing their apparent proportion. In this series, 18 cases were not diagnosed by *x*-ray examination. In six of these no barium-meal study was performed at any time before surgery or necropsy disclosed the ulcers. In most cases an emergency situation such as bleeding or perforation was responsible for this omission. In another six cases the last radiological investigation had taken place two to six years before gastric surgery revealed an additional ulcer not shown before. Judging from the symptoms during the interval, the presence of combined ulcers at the previous examination is unlikely. In only five patients was one of the ulcers certainly missed. There were duodenal scars in four of these patients, and an active duodenal ulcer in one, accompanied by a considerable degree of pyloric stenosis. In addition, one gastric ulcer was possibly not detected two months before it was found at an emergency operation for bleeding. In no case examined radiologically were both ulcers missed. Thus the *x*-ray findings were incomplete in less than 5%. It is believed that careful *x*-ray examination provides reliable data for estimating the incidence. The high proportion of positive diagnoses reflects the particular care taken in the hospital's *x*-ray department in respect of barium-meal studies as well as the awareness of the frequent concomitance of ulcers. In the majority of cases the radiological diagnosis was confirmed by surgery or gastroscopy or both.

Time Sequence of Ulcer Appearance

The sequence is of some importance in aetiological considerations on combined ulceration. Previous observations by Feldman (1953) and Johnson (1955) showed that a proved chronic duodenal ulcer preceded the appearance of the gastric ulcer in most patients. This sequence took place in 91 patients (group 1), of whom 20 were women (Table II).

TABLE II.—*Sequence of Ulcer Appearance and Sex Incidence*

Group	Sequence	Total	Men	Women	Sex Ratio
1	D.U.→G.U.	91	71	20	3·6 : 1
2	"Simultaneous" G.U.+D.U.	25	19	6	3·2 : 1
3	Sequence unknown ..	20	17	3	5·7 : 1
4	D.U.→G.E.→G.U.* ..	13	11	2	5·5 : 1
5	G.U.→D.U.	8	7	1	7 : 1
	All groups	157	125	32	3·9 : 1

* Including one vagotomy without gastro-enterostomy.

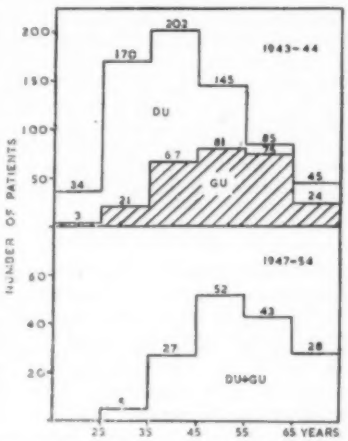
In 25 others the ulcer history was remarkably short, rarely exceeding two months. Still the first *x*-ray examination or surgery performed for complications showed both active duodenal and gastric ulcers (group 2). No sequence could be established in 20 patients with incomplete records or in cases where a long ulcer history preceded the first *x*-ray study which showed combined ulcers (group 3). Twelve patients underwent gastro-enterostomy for duodenal ulcer 1 to 25 years before a gastric ulcer at some distance from the anastomosis was discovered (group 4). Another patient also included in this group had submitted to a vagotomy without gastro-enterostomy for duodenal ulcer two years before an ulcer of the stomach appeared. Similar cases have been reported by Johnson (1955).

Evidence for a gastric ulcer preceding a duodenal ulcer was obtained in eight patients (group 5). The early *x*-ray films of these patients were reviewed by the radiologist, and the duodenal cap was found to be normal in the presence of a gastric ulcer in all instances.

Sex and Age Incidence

Of the 157 patients with combined ulcers, 32 were women, giving a sex ratio of 3.9:1 (Table II). This figure lies between the ratios of 2.4:1 in respect to gastric and 6.8:1 in respect to duodenal ulcers found during a somewhat earlier period at the Central Middlesex Hospital (Avery Jones and Pollak, 1945). There was little variation of this ratio in the different age groups in either this or the present study. Deviations in the small groups may be due to an inadequate number of cases.

The age incidence is represented in the lower half of the Chart, which shows the distribution at the time both ulcers were recognized. For comparison, the age distribution of duodenal and gastric ulcers at the same hospital is included in the upper half (Avery Jones and Pollak, 1945). It is readily seen that the age distribution in combined ulcers is very similar to the gastric ulcer group.



Age distribution. Top: duodenal and gastric ulcers (Avery Jones and Pollak, 1945). Bottom: combined ulcers.

In patients with duodenal ulcer preceding gastric ulcer (group 1) the mean age at which the combined lesion was diagnosed was 54 years, with little variation between the sexes. Symptoms of peptic ulcer appeared at the much earlier age of 39 years on the average. However, the diagnosis of duodenal ulcer usually was established much later, after an interval averaging almost eight years. Many of the patients showed no free interval before the gastric ulcer appeared, making it impossible to date the onset of the latter. In some, however, there was either a relapse following a prolonged remission or a definite change in the character of the disease, and in these the interval between onset of symptoms and *x*-ray or surgical confirmation of gastric ulceration was quite short.

In the other groups the mean age at the time both ulcers were discovered similarly lies between 50 and 55 years. In group 5 the gastric ulcer was diagnosed on the average six years before the duodenal ulcer. Intervals ranged from some months to 14 years.

Characteristics

Activity.—As judged by definite *x*-ray demonstration of an ulcer crater or by surgery, both ulcers were active together at any one time in 98 of the 157 patients. This incidence of almost two-thirds may reflect the severity of the disease in this series.

Free Interval.—A symptom-free interval lasting more than one year was present in 41 patients. This figure applies to the 112 patients with a known sequence only (groups 1, 4, and 5). In the eight cases showing the gastric-duodenal ulcer sequence (group 5) any free interval was always shorter than one year.

Change in Symptoms.—Most symptoms besides pain were too indefinite to allow investigation. Excluding groups 2 and 3 ("simultaneous" appearance or unknown sequence) as well as cases with incomplete records in this respect, enough notes on pain were available in 89 patients. Some definite change was noted in 42 of these, being a change in character of pain only in 29, a shift in site only in another 3, and a change in site as well as character in 10 patients. It appears

that in a minority only can combined ulceration be suspected on the basis of change in symptoms. The significance of vomiting is discussed below.

Site of Gastric Ulcer.—The ulcer was located at the angulus in 45 cases, at the middle third of the lesser curve in 82, and at the upper third in 30. In the presence of multiple ulcers the lesion appearing first was taken into account. No relation of the ulcer site to either age or sex could be established.

Multiple Ulcers.—These were present in 22 cases, with two gastric ulcers in nine cases, three gastric ulcers in three, and four gastric ulcers in one. Kissing duodenal ulcers were observed in nine instances.

Gastric Retention

With regard to pyloric stenosis, the following groups were established. (A) Occasional or no vomiting; no *x*-ray evidence of delayed emptying. (B) Frequent but transitory vomiting; little vomiting with considerable loss of weight; no *x*-ray evidence of delay. (C) Delayed emptying, later followed by normal emptying on *x*-ray investigation. (D) Pyloric stenosis, predominantly organic in nature, as a rule treated surgically.

Table III shows the respective distribution. Not included among the 131 cases are the patients with a former gastro-enterostomy. In these no delay in emptying appeared to be present, and some factor other than retention might be

TABLE III.—*Incidence of Gastric Retention*

Presence and Degree of Gastric Retention	No. of Patients	Incidence
A. No or rare vomiting; normal emptying	94	71·7%
B. Frequent vomiting or weight loss; normal emptying	12	9·2%
C. Transitory delay in emptying	13	9·9%
D. Organic pyloric stenosis	12	9·2%
Total (cases with gastric-duodenal sequence and G.E. or vagotomy excluded)	131	100%

responsible for gastric ulcer formation. Also excluded are the eight cases with the unusual gastric-duodenal-ulcer sequence and five cases with insufficient details. In group A gastric retention was presumably never present, and thus would not appear to play any part in the appearance of the gastric ulcer in more than 70% of the series. Even this figure may represent a conservative estimation, because it is by no means certain that frequent vomiting or loss of weight is indicative of decreased emptying. Severe pain and even fear of pain may give rise to both.

Other Complications

Of the 157 patients, 59 had a total of 89 haemorrhages. This incidence has to be considered in relation to duration of the disease as shown in Table IV. In the group of 91 patients with the known duodenal-gastric-ulcer sequence, nine suffered from haemorrhages while they had a duodenal ulcer only, the disease lasting on the average 12½ years. At

TABLE IV.—*Incidence of Bleeding in Single and Combined Ulcers Related to Duration of Disease*

	No. of Patients	Patients with Haemorrhage		No. of Haemorrhages	Average Duration of Disease in Years
		No.	%		
Duodenal ulcer (Group 1 only*)	91	9	10	11	15 {with haem., 12·5; without haem. 16·4}
Combined ulcers (Group 1 only*)	91	27	30	36	1·4 {with haem., 1·1; without haem., 1·6}
Combined ulcers (all groups)	157	45	29	64	1·6
Total	157	59	38	89	13

* See Table II.

the time combined ulcers appeared there were 36 instances of bleeding in 27 patients. The haemorrhages then took place in a period barely exceeding one year. The gastric ulcer was proved to be the source of bleeding in 16 of these patients, while the others may have bled from either stomach or duodenum. Thus the incidence of bleeding appears much higher in the presence of combined ulcers in spite of their short coexistence.

In many instances the combined ulcer disease was terminated by partial gastrectomy, often after the first haemorrhage. This would alter the proportion of haemorrhages in respect of time. To obviate this difficulty a special group of 49 patients was investigated. These 49 cases could be followed for a period of at least one year after the diagnosis of gastric ulcer following duodenal ulcer was established by *x*-ray examination. Six patients suffered from a total of eight haemorrhages while they supposedly had a duodenal ulcer only, the disease lasting 722 patient-years in the 49 cases. On the other hand, during the period of combined ulceration with 130 patient-years, the number of haemorrhages was 12, with 10 patients bleeding. Thus there was one haemorrhage for 90 patient-years with single as compared with one for 11 patient-years with combined ulcers in this group. These findings correspond reasonably well with the data of all patients with the same sequence.

Age was not responsible for an increased incidence of bleeding, the patients with haemorrhages being on the average four years younger at the time both ulcers were discovered.

In all groups taken together there were 89 haemorrhages in the 157 patients, and at least every third patient bled at one time or another. Although in several instances it was difficult to correlate the bleeding accurately with the presence of either single or combined ulcers, in 45 patients at least the haemorrhage took place when both gastric and duodenal ulcers were present. Here again the much higher incidence is apparent, inasmuch as the bleeding took place during a period averaging little more than one and a half years. Some patients, however, may have bled from a lesion other than a gastric or duodenal ulcer, particularly in the group with a previous gastro-enterostomy.

The 24 perforations in 22 patients were with one exception duodenal. There were nine cases of hourglass deformity of the stomach.

If pyloric stenosis is included, 92 of the 157 patients thus suffered from one or more major complications—again a striking proportion. The complications are listed in Table V.

TABLE V.—*Complications, Operations, and Deaths in 157 Patients With Combined Ulcers*

		No. of Patients	Incidence
Gastric retention	Possible	12*	9%*
	Proved	25*	19%*
Haemorrhage		59	38%
Perforation		22	14%
Hourglass stomach		9	6%
One or more complications		92	59%
Operations	Partial gastrectomy	68	43%
	All types	82	52%
Deaths		5	3%

* Of 131 patients (see Table III).

Deaths

During the eight-year period there were five known deaths more or less directly due to the ulcer disease. The causes of death were as follows. One patient died from bronchopneumonia after a successful partial gastrectomy for active duodenal and gastric ulcers at the age of 68. Subacute bowel obstruction four months after gastrectomy required another operation, from which the patient did not recover. A second fatality related to surgical treatment occurred in a man aged 53 operated on for both gastric and stomal ulcers

after a gastro-enterostomy established 15 years earlier for duodenal ulcer. Death took place following reoperation necessitated by bleeding shortly after partial gastrectomy. Another patient, aged 69, had well recovered after suture of a perforated duodenal ulcer, but died suddenly from massive bleeding due to chronic gastric ulcer. A fourth male patient with a 30-year history of peptic ulcer died two years after a successful partial gastrectomy. At necropsy, renal disease suggestive of Burnet's syndrome due to prolonged alkali medication was found. The fifth patient, a man of 60, died 24 hours after emergency admission for a bleeding gastric ulcer accompanied by a duodenal scar.

Operation

Of the 157 patients, 82 underwent one or more operations for peptic ulcer, including simple suture for perforation and gastro-enterostomy. Several patients were operated on twice. In 68 partial gastrectomy was performed. In at least eight cases this was done as an emergency measure for bleeding. Forty patients undergoing gastrectomy were over 50 years of age, and, among these, 24 were more than 60 years old.

Gastric Secretion.—The available data on 79 patients could not be compared, because gastric secretion had been assayed by different methods.

Discussion

A radiological diagnosis of combined gastric and duodenal ulcers was made in 2.7% of more than 5,000 ulcer patients in the eight-year period 1947–54. Inclusion of an estimated 25% of prepyloric ulcers would raise this figure to 3.5%. This is in fair agreement with the findings of Morrison and Feldman (1951), who in a special investigation observed clinical and radiological evidence of combined ulcers in 4.2% of 500 peptic ulcer patients. A considerably lower proportion was reported in most general *x*-ray and post-mortem series reviewed by Feldman (1953). Papers not mentioned by this author include those by Needham and McConachie (1950), Shapiro and Schiff (1952), and Stewart, Sanderson, and Wiles (1952) indicating that 1.8 to 4% of bleeding gastric and duodenal ulcers show combined lesions. Smith, Boles, and Jordan (1953) found a concomitant duodenal deformity in 19.7% of patients with benign gastric ulcers of all sites. Glenn and Harrison (1951) reported 12% and Rauch (1952) 3.2% of combined ulcers in their surgical patients. Johnson (1955) personally observed concomitant lesions in one of seven duodenal and one of four gastric ulcer patients. He suggested a general incidence of about 5%, including asymptomatic cases. There is reason to believe that the higher incidence generally reported by surgeons may be caused by the selection of patients.

No doubt the most reliable figures on combined ulcers are to be found in Watkinson's (1958) analysis of the necropsy findings in the late Professor Matthew Stewart's department at the University of Leeds. The incidence reported here is by far the highest with the exception of Sir David Wilkie's findings in 1926. This is explained by the painstaking care taken in the department in the detection of all ulcers and ulcer scars. Of a total of 1,848 chronic ulcers found between the years 1930 and 1949, 227 were combined gastric and duodenal ulcers, 174 in men and 53 in women. The calculation of the incidence is best based, however, on the findings in patients who died from causes other than ulcer disease. There were 1,232 of these patients, and 142 showed combined lesions. This gives an incidence as high as 11.5%. In the same group there were 799 duodenal and 284 gastric ulcers. The proportion of combined lesions among gastric ulcers (284+142) thus reaches 33.4%, and among duodenal ulcers (799+142) 15.1%. The sex ratio of combined ulcers in patients not dying from their ulcers was found to be 1.58 compared with 1.97 in the duodenal and 1.09 in the gastric ulcer groups, the male patients always predominating. The greatest incidence was found between the ages of 45 and 74 in males and above the age of 75 in females.

Admittedly a study based on hospital in- and out-patients will not allow any conclusions as regards the incidence of the disease in the general population. In hospital patients at least, the incidence is certainly high. As already pointed out by Johnson (1955), this is surprising, because many features of duodenal and gastric ulceration are to some extent mutually exclusive. The differences in gastric secretion between duodenal and gastric ulcer patients are well known. Differences in the motor activity of the stomach and duodenum are not as well documented as the secretory aspects. Most patients with uncomplicated duodenal ulcer are found on gastric biopsy to have a normal stomach mucosa. On the other hand, the incidence of gastritic changes in the ulcer-bearing stomach is high. Such features may appear compatible in cases where the gastric ulcer follows a healed duodenal ulcer after a long interval. However, almost two-thirds of the present cases showed active lesions of both stomach and duodenum. Moreover, in at least eight cases the reverse sequence occurred. On occasion the evolution was quite striking, the gastric and duodenal ulcer appearing to be independent of each other.

Thus in a man aged 40 with a short history of dyspepsia a large ulcer was found at the middle third of the lesser curve. He was successfully treated as an in-patient and four *x*-ray series did not reveal any duodenal crater or deformity. A few days after he left the hospital he was readmitted for a perforated duodenal ulcer, which was sutured. No active gastric lesion was found at the operation. The duodenal ulcer healed, but the gastric ulcer relapsed within three months. One year later the duodenal ulcer had also recurred, accompanied by two gastric ulcers. When partial gastrectomy was performed after another two months, the gastric ulcers had healed. At no time was there any evidence of delayed emptying. The pattern of gastric secretion did not change markedly when concomitant ulceration followed the gastric ulcer.

That even the pattern of gastric secretion may change is shown in observations reported by Watkinson (1951). In one 42-year-old male patient the healing of a gastric ulcer was followed within five months by the appearance of a duodenal ulcer, both confirmed at operation. In another man aged 33 a gastric ulcer appeared six months after a duodenal ulcer had healed. In both patients there was a definite change in gastric secretion from the gastric ulcer type to the pattern found in duodenal ulcer, and vice versa.

Gastric retention is one factor thought to be responsible for combined ulceration (Johnson, 1955). In less than 30% of the 131 patients analysed in this respect were there any possible signs of pyloric stenosis. Even in cases with delayed emptying it may be questioned whether gastric retention is the cause rather than the effect of chronic gastric ulceration. Retention is present in a similar proportion of gastric and duodenal ulcers. The importance of pyloric stenosis arising from duodenal ulcer may also be questioned on the basis of the sex ratio, which was nearer to the figure found in gastric ulcer. Again the age distribution is more or less the same as in gastric ulcer. It is thought that a factor common to both gastric and duodenal ulcer disease may be at work to cause combined ulcers. Unfortunately, there was insufficient material for a detailed analysis in respect of ulcer inheritance. In several instances, though, the family history was most striking, with proved cases of both gastric and duodenal ulcers in near relatives of the patients. The work of Doll and Kellock (1951), which includes cases with combined ulcers, is most suggestive of a common hereditary background. They observed that 6 out of 11 patients with combined ulcers had near relatives with the same disease.

It is reasonable to expect that combined ulcer disease runs a more severe course than either duodenal or gastric ulcer. Although no conclusive proof can be offered, the present study bears out this impression. The proportion of patients with perforations is not unexpected in view of the findings of Martin and Lewis (1949). On the other hand, the risk of bleeding is certainly high, particularly if

the period before the appearance of combined ulcers is taken as a basis for comparison. According to Balfour (1932) about 25% of peptic ulcer patients followed for an average of 10 years will show one or more episodes of bleeding. Emery and Monroe (1935) found an incidence of 26.7% in patients observed for an average of 3.5 years. Gastric ulcers are thought to bleed more often than duodenal ulcers (Ivy, Grossman, and Bachrach, 1950). However, Martin and Lewis (1949), in their follow-up of peptic ulcer patients for more than 10 years, observed bleeding in 26.8% of gastric and 35.2% of duodenal ulcers. In the present series the incidence of bleeding in 59 of 157 patients—that is, 37.6%—followed for a similar length of time, is somewhat higher. Moreover, three-fourths of the haemorrhages took place during the period which represented on the average one-eighth or less of the total ulcer history. It is therefore not surprising that conservative treatment was abandoned in favour of partial gastrectomy in 68 of these patients. In fact, the present findings would suggest that surgical treatment is indicated more often in combined ulcers than in single ulcer, whether gastric or duodenal.

Summary

The combination of chronic gastric and duodenal ulcers or ulcer scars was found in 157 hospital patients during a period of eight years. Cases suffering from prepyloric gastric ulcer were excluded owing to the uncertainty of location.

The observed incidence of combined ulceration was 2.7% based on *x*-ray investigation. With the inclusion of an estimated 25% of prepyloric ulcers the incidence would reach 3.5%. Thus about one in every seven hospital patients suffering from ulcers of the stomach and 1 in 30 patients having a duodenal ulcer or ulcer scar will be found to show combined ulcers.

With due awareness of the frequent occurrence of combined ulcers, the radiological examination represents a reliable means of their diagnosis.

Combined ulcers run a higher risk of bleeding, making surgical treatment more often advisable than in either gastric or duodenal ulcer occurring alone.

Pyloric stenosis does not appear to be a major factor in the pathogenesis of combined ulcers.

I wish to thank Dr. F. Avery Jones, Dr. R. Doll, and Dr. T. D. Kellock, in whose department this work was done, for much encouragement and advice. Dr. F. Pygott kindly made his files available and reviewed several *x*-ray films. I am also indebted to the clerical staff of the Central Middlesex Hospital. The work was done during the tenure of a fellowship of the Swiss Foundation for Fellowships in Biology and Medicine.

References

Balfour, D. C. (1932). *Ann. Surg.*, **96**, 581.
Doll, R., and Kellock, T. D. (1951). *Ann. Eugen. (Lond.)*, **16**, 231.
Emery, E. S., and Monroe, R. T. (1935). *Arch. intern. Med.*, **55**, 271.
Feldman, M. (1953). *Gastroenterology*, **23**, 304.
Glenn, F., and Harrison, C. S. (1951). *A.M.A. Arch. Surg.*, **62**, 151.
Gott, J. R., Shapiro, D., and Kelty, K. C. (1954). *New Engl. J. Med.*, **250**, 499.
Ihre, B. J. E., and Müller, R. (1943). *Acta med. scand.*, **116**, 33.
Ivy, A. C., Grossman, M. I., and Bachrach, W. H. (1950). *Peptic Ulcer*. Blakiston, Philadelphia.
Johnson, H. D. (1955). *Lancet*, **1**, 266.
Jones, F. A., and Pollak, H. (1945). *Brit. med. J.*, **1**, 797.
Martin, L., and Lewis, N. (1949). *Lancet*, **2**, 1115.
Morrison, S., and Feldman, M. (1951). *Amer. J. dig. Dis.*, **18**, 296.
Needham, C. D., and McConachie, J. A. (1950). *Brit. med. J.*, **2**, 133.
Rauch, R. F. (1952). *Surgery*, **32**, 638.
Shapiro, N., and Schiff, L. (1952). Ibid., **31**, 327.
Smith, F. H., Boles, R. S., and Jordan, S. M. (1953). *J. Amer. med. Ass.*, **153**, 1505.
Stewart, J. D., Sanderson, G. M., and Wiles, C. E. (1952). *Ann. Surg.*, **136**, 742.
Watkinson, G. (1951). *Gastroenterology*, **18**, 377.
—— (1958). *Schweiz. Z. allg. Path.*, **21**, 405.
Wilkie, D. P. D. (1926). *Brit. med. J.*, **2**, 469.

RECTAL TEMPERATURE IN THE NEWBORN AFTER BIRTH ASPHYXIA

BY

E. D. BURNARD, M.B., M.R.C.P., M.R.A.C.P.

AND

K. W. CROSS, Ph.D., M.B., M.R.C.P.

Paediatric Unit and Physiology Department, St. Mary's Hospital Medical School, London

In a previous investigation (Cross, Tizard, and Trythall, 1955) it was shown that if normal babies were given 15% oxygen to breathe there was a fall in oxygen consumption which was so large that the energy loss would be greater than the energy gain from any anaerobic metabolism which might be taking place. From this indirect calorimetry it was suggested that energy production fell under these experimental conditions, and this seemed to be confirmed when Brodie, Cross, and Lomer (1957) showed that infants breathing 15% oxygen heated the plethysmograph in which they were placed less than when they breathed air, though a consistent fall in rectal temperature was not found when the 15% oxygen was given for periods up to 50 minutes. Young kittens and puppies show a fall in temperature directly after oxygen consumption is reduced in anoxia (Moore, 1956a, 1956b).

In babies the absence of this immediate fall in body temperature along with their fall in oxygen consumption in an atmosphere of 15% oxygen might be connected with a relative thermal inertia compared with the smaller animals. Vascular reactions might also play a part, since skin pallor was noticed in the babies. The probability that factors such as these influenced the findings in short-term observations is supported by Sjöstedt and Rooth's (1957) report that in full-term babies the temperature is "a little lower than normal if kept in 15% oxygen for a week."

Although suggestive, these results might not apply to the infant showing apnoea or cyanosis at or after birth. While cyanosis is evidence of anoxia, it is unlikely that the natural condition is ever a pure "anoxic anoxia." CO_2 retention will probably, although not necessarily, be present. An investigation which would in some measure test whether naturally occurring anoxia causes a fall in heat production of the newborn infant was undertaken. We wished to make the investigation as simple as possible so that it could be fitted into the activities of a busy maternity unit, and decided to divide the babies into those that did and those that did not show asphyxia at birth, and to follow their rectal temperatures. As it became apparent that maternal sedation was a complication the scope of our investigation had to be widened slightly, and finally four groups of infants were studied, but the general scheme was not made more complex in any other way.

Material and Methods

Babies were delivered at a labour-room temperature of 78–80° F. (25.6–26.7° C.), wrapped in a towel, and, after they had been held by their mothers, were transferred to the nursery after a period that varied from 10 to 30 minutes. Resuscitative measures used after birth were oxygen, which was given for a few minutes at the discretion of the obstetrician or midwife in charge, and 1 mg. of N-allyl

morphine by intramuscular injection if delay in breathing could be attributed to maternal sedation with pethidine; some mothers who had received pethidine were given 10 mg. of N-allyl morphine an estimated 30 minutes before delivery. In the nursery, where the temperature was kept between 70 and 74° F. (21.1 and 23.3° C.) throughout the investigation, the infant was covered with two blankets, and, after a further interval varying between half an hour and one and a half hours was bathed and dressed.

The rectal temperature was taken two-hourly for 24 hours by the nursing staff with thermometers graduated from 85 to 105° F. (29.5 to 40.6° C.), the thermometer being inserted an inch (2.5 cm.) beyond the anus. A complete record was not always obtained, as will be apparent from inspection of the individual totals in Figs. 1–3. So far as possible, all the babies born in a four-months period were examined, but at busy times the taking of temperatures had to lapse.

The infants were born at term, or possibly later in a minority. None received any special treatment apart from oxygen for the few minutes before the establishment of normal breathing. Babies who needed oxygen for some hours after birth have been excluded from this report.

Asphyxia in this paper means failure to establish respiration within three minutes of birth. While the observations were being made it became clear that maternal sedation with pethidine was a frequent cause of apnoea, and a division was therefore made into the following groups: A ("normals"), 53 babies whose breathing began within three minutes and the mother had received only chloral; B ("pethidine and apnoea"), 29 babies in whom normal breathing was not established within three minutes, the mothers having received pethidine; C ("pethidine, no apnoea"), 35 babies who were breathing normally within three minutes, all the mothers having received pethidine. Group D ("pure asphyxia") is made up of 15 babies. The need for sedation in difficult labour rendered apnoea after birth without maternal pethidine an uncommon event, and explains the small number of observations in this group.

The dosage of pethidine and the time between administration to the mother and birth varied considerably. In order that an infant should qualify for groups B or C it had to be born within three hours of a single dose of 200 mg. or within five hours after 400 mg. (2×200 mg.) or more.

The accompanying charts show the mean temperatures for each group, and the vertical lines indicate the 95% confidence limits for each set of two-hourly observations. When there is no overlapping of these lines the odds against the difference between means being due to chance are greater than 20 to 1.

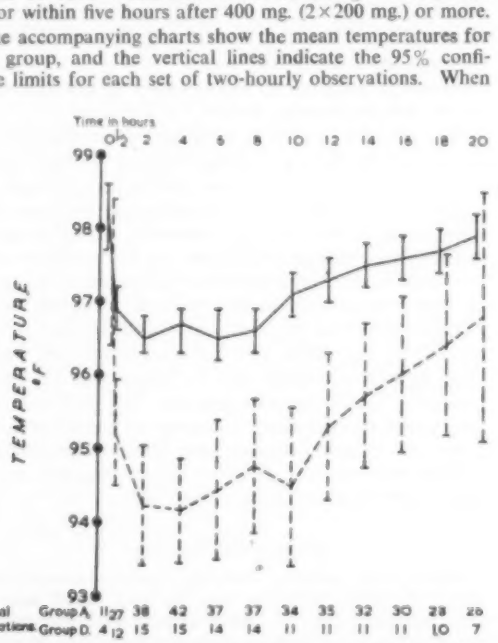


FIG. 1.—Mean rectal temperatures after normal birth and after birth asphyxia. The vertical lines are the 95% confidence limits of the means. ——— Group A (normals), 53 babies. ------ Group D (asphyxia, no pethidine), 15 babies.

Results

In Fig. 1 the means of groups A and D are compared. Asphyxia is seen to result in a significantly lower rectal temperature from the second to the sixteenth hour.

In Fig. 2, group B is compared with the normal, and a significant lowering of temperature over the same period is apparent. In group C, however, the fall in temperature occurred after pethidine without the intervention of apnoea (Fig. 3), and it is for this reason that we were careful to exclude the possibility of a drug effect in collecting the data for Fig. 1.

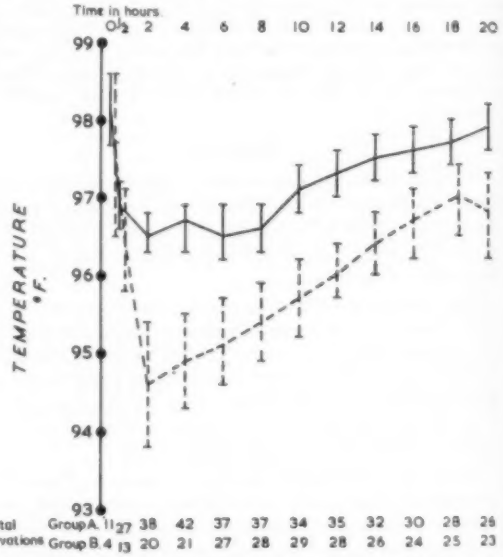


FIG. 2.—Mean rectal temperatures after maternal pethidine and apnoea at birth. Conventions as in Fig. 1. ——— Group A (normals), 53 babies. ------ Group B (pethidine and apnoea), 29 babies.

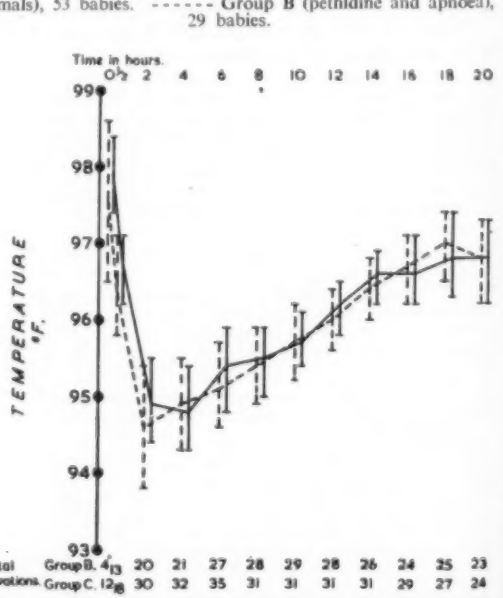


FIG. 3.—Comparison of mean rectal temperatures after maternal pethidine with and without apnoea at birth. Conventions as in Fig. 1. ------ Group B (pethidine and apnoea), 29 babies. ——— Group C (pethidine, no apnoea), 35 babies.

Group C comprised 18 babies who received N-allyl morphine, and 17 who breathed in three minutes without it. These subgroups were analysed separately, and as there was very little difference between them they have been taken together to give the total 35 group C babies. The failure of N-allyl morphine, used as an antidote to pethidine apnoea, to influence the later temperature is the subject of comment below.

There was no clinical disorder in any of the babies, apart from the need for brief resuscitative measures at birth in a minority of the apnoeic ones, as has already been noted. Cyanosis both of the lips and of the extremities occurred to a varying degree, as did variations in respiratory rate.

Discussion

The fact that there is a significant difference in temperature over several hours between group A and group D suggests that asphyxia causes a fall in oxygen consumption and energy production as in the experiments on pure anoxia (15% oxygen) already quoted. It is worth speculating on the degree of anoxia our subjects had met, as Brodie *et al.* noted no fall in rectal temperature in infants breathing 15% oxygen for 50 minutes. The pronounced fall in heat production suggested by the low rectal temperature points to an incident of considerable severity.

There is no apparent difference between the temperatures of the two groups of babies whose mothers had received pethidine (B and C), whether the babies were apnoeic for three minutes after birth or not. Their pattern of temperature change after birth is very similar to that of babies with pure asphyxia. Either the initial asphyxia or mild persisting respiratory depression from the drug could explain the similarity to the group D babies. A second possibility is vasodilatation, since J. Ginsburg (1958, personal communication) has found an approximate doubling of skin-blood flow in the human subject for periods up to an hour after 100 mg. of pethidine intramuscularly. Thus the temperature of babies after maternal pethidine might be lowered both by diminished heat production and by increased heat loss.

To some extent the absence of a difference between groups B and C may be due to artificial selection, because severely asphyxiated babies who were felt to need oxygen for a number of hours after birth have not been included in the series, although some of them had much lower temperatures and these would have enlarged group B.

When the babies in group C were divided according to whether or not they had received N-allyl morphine, the fall in temperature was the same in each subgroup. While the drug proved a very effective antidote to pethidine in the initiation of breathing (Paterson and Prescott, 1954) it did not appear to have any subsequent effect on the course of temperature. Roberts *et al.* (1957) similarly found that the reduction of the baby's minute-volume after maternal pethidine was not influenced by this antidote.

We conclude that a somewhat reduced rectal temperature is a natural phenomenon in babies suffering from asphyxia at birth. It seems probable that this lowered temperature is the result of a period of diminished metabolic rate, caused by the anoxia. If this is so, then the lower temperature may have survival value.

Summary

Neonatal rectal temperature was measured at two-hourly intervals in 53 infants after normal delivery and in 15 after birth asphyxia. Asphyxia was found to cause a significantly lower temperature for 16 hours.

The same effect followed the maternal administration of pethidine independently of apnoea at birth.

The reduced temperature appears to be a natural consequence of anoxia in the baby.

We thank Mr. Leslie Williams, Mr. Douglas MacLeod, and Dr. Reginald Lightwood for permission to examine infants in their care, and Sister K. A. Taylor and her nursing staff for their faithful co-operation.

REFERENCES

Brodie, H. R., Cross, K. W., and Lomer, T. R. (1957). *J. Physiol. (Lond.)*, **138**, 156.
Cross, K. W., Tizard, J. P. M., and Trythall, D. A. H. (1955). Ibid., **129**, 69P.
Moore, R. E. (1956a). Ibid., **131**, 27P.
—— (1956b). Ibid., **133**, 69-70P.
Paterson, S. J., and Prescott, F. (1954). *Lancet*, **1**, 490.
Roberts, H., Kane, K. M., Percival, N., Snow, P., and Please, N. W. (1957). Ibid., **1**, 128.
Sjöstedt, S., and Rooth, G. (1957). *Arch. Dis. Childh.*, **32**, 397.

TREATMENT OF RHEUMATOID ARTHRITIS WITH CHLOROQUINE

BY

H. FULD, M.D., M.R.C.P.Ed.
Consultant Physician

AND

L. HORWICH, M.B., Ch.B.
Medical Registrar
Sefton General Hospital, Liverpool

Mepacrine was first observed to have a beneficial effect on the course of rheumatoid arthritis by Page (1951), when treating discoid lupus erythematosus. Two of these patients had associated rheumatoid arthritis, which cleared up under mepacrine treatment. Haydu (1953) two years later published his result of treatment by chloroquine of 28 patients suffering from rheumatoid arthritis. In the dosage of 0.5 g. of chloroquine thrice weekly for six months he found considerable improvement in 21 of the 28 patients with rheumatoid arthritis without encountering toxic symptoms during the trial. Forestier and Certonciny (1954) published a short-term trial of mepacrine in 11 patients and of chloroquine in 17 patients suffering from rheumatoid arthritis for a period of one to six months. Half of the patients in each group responded favourably. Escarpenter-Oriol *et al.* (1955), quoted by Bagnall (1957), treated eight rheumatoid arthritics with mepacrine and 30 with chloroquine, but none of them received more than five months' treatment. Nevertheless, the authors noted an improvement in 29 of the chloroquine cases.

Following an investigation of the unusually high incidence of amoebic infection in patients with rheumatoid arthritis (95% compared with 30% of normal patients in Oregon), Rinehart employed chloroquine together with di-iodohydroxyquinoline ("diodoquin") in these patients (Rinehart, 1955; Rinehart *et al.*, 1957). He noted improvement in both conditions and attributed most of the antirheumatic activity to chloroquine. Eight out of 11 children showed major improvement of rheumatoid arthritis, and 8 out of 14 adults experienced similar benefit. He followed this series by a "double blind study" of two groups of rheumatoid arthritics (33 in all) receiving either chloroquine or an inert substance. He regarded the improvement in the chloroquine group as statistically significant, more than half the patients on chloroquine deriving and maintaining improvement after two months.

Freedman (1956) observed 66 patients, divided into equal groups of similar rheumatoid disease, half of whom received chloroquine (200 to 300 mg. a day) and the remainder dummy tablets. Small doses of salicylates were permitted during the trial, which lasted 16 weeks in the first instance. Subjective and objective progress was assessed and there was appreciable benefit during this period. Subsequently, 50 patients remaining under treatment received chloroquine and 43 became really

well. Nausea and vomiting and mild dermatitis were the only toxic effects noted in this group, and necessitated some reduction in dosage. Lacapère *et al.* (1954) treated 80 long-standing cases of rheumatoid arthritis with chloroquine in doses up to 600 mg. daily and reported favourable results in two-thirds of these patients.

A much larger number of patients suffering from rheumatoid arthritis have been treated and observed over the long period of four years by Bagnall (1957). He followed up personally 125 private patients, of whom 121 had more than eight months of continued therapy and 25 received treatment for longer than three years. He stressed that no early response to chloroquine was to be expected and that no benefit may be obtained prior to 6 to 12 weeks after the beginning of treatment. To bridge this period, rest, sedation, salicylates, and when necessary glucocorticoid therapy were used. There was a good result in 70% as judged by work performance, sedimentation rate, and haemoglobin level. Six patients relapsed on premature withdrawal of the drug but benefited when treatment was resumed. Only minor toxic symptoms were encountered. 10% were unable to continue the drug. He concluded that "chloroquine comes closer to the ideal for a long-term safe control of rheumatoid arthritis than any other agent now available." Scherbel *et al.* (1957, 1958) administered chloroquine phosphate or hydroxychloroquine sulphate to 716 patients suffering from rheumatoid arthritis over periods up to three years. They have so far reported their results in 157 patients. A major improvement occurred in 58%. The Table represents a summary of the results of chloroquine treatment of rheumatoid arthritis published up to April, 1958.

Literature on Antimalarial Drugs in 1,092 Cases of Rheumatoid Arthritis

Author	No. of Patients	Length of Treatment	Drugs	Results
Page (1951)	2	1–3 months	Mepacrine	Improvement in both cases
Haydu (1953)	28	6 ,,	Chloroquine	75% considerable improvement
Forestier and Certonciny (1954)	28	1–6 ,,	11 Mepacrine 17 Chloroquine	50% improved
Lacapère *et al.* (1954)	80		Chloroquine	60% improvement
Escarpenter-Oriol *et al.* (1955)	38	Up to 5 months	8 Mepacrine 30 Chloroquine	97% improved in chloroquine group
Rinehart (1955), Rinehart *et al.* (1957)	25		Chloroquine + diodoquin	65% improvement
Freedman (1956)	50		Chloroquine	86% improvement
Bagnall (1957)	125	30% less than 6 months; 97% from 8 months to over 3 years	,,	70% considerable improvement
Scherbel *et al.* (1958)	716	Up to 3 years	Hydroxychloroquine Chloroquine	58% major improvement (157 patients)

Present Series

Our own experience of chloroquine in hypersensitivity states and collagen diseases dates back to July, 1953, when one of us (H. F.) first tried the drug in systemic lupus erythematosus followed by other collagen diseases and hypersensitivity states (1958). In 1954 we began to treat cases of active rheumatoid arthritis with chloroquine, but were quite sceptical about any possible benefit, and it was not until 1955 that we were convinced that chloroquine influenced the course of the disease, and it was from then on that we followed these cases up regularly. Thirty-nine patients (29 female, 10 male) were observed between May, 1955, and August, 1958, the longest for up to four years and the most recent patients for only three months. The average duration of symptoms prior to the commencement of chloroquine treatment varied between several years in almost half the cases to a few months in three patients. No patient with "burned-out" arthritis was treated. The indications for chloroquine therapy were painful joint swellings and muscle spasm accompanied by a raised E.S.R. and low-grade pyrexia. With few exceptions our patients had had previous treatment elsewhere, including gold injections, steroid hormones, and phenylbutazone, and one patient had had deep *x*-ray therapy for ankylosing spondylosis. None of these measures gave lasting relief.

We soon found that no benefit from chloroquine could be expected for some three weeks from the start of treatment, and almost all patients therefore received other therapeutic measures soon after admission. These comprised the following. (1) Salicylates in the form of calcium aspirin for symptomatic relief. (2) Complete bed rest for several weeks or until the E.S.R. returned to normal. (3) Artificial fever by means of intravenous T.A.B. vaccine in four doses starting with 25 million and increasing to 100 million organisms at intervals of three to four days. Thirteen patients received the full course. (4) Weekly transfusions of 1 pint (570 ml.) of fresh blood in 11 patients over a period of three to four weeks. (5) Injection of hydrocortisone acetate into single joints to overcome deformities by relief of muscle spasm. (6) Graded physiotherapy after acute stage.

One of us (H. F.) has used this regime of treatment of active rheumatoid arthritis for many years; quite often satisfactory remissions followed, but relapses occurred in most cases sooner or later. Chloroquine was started on admission to the ward or at the end of induced fever treatment. The initial dosage was 600 mg. daily, and was reduced only when gastric irritation made it necessary.

Of the 39 patients, all but five still take a maintenance dose of chloroquine 200 to 400 mg. daily. Two discontinued the drug because of lack of benefit and three could not tolerate prolonged treatment on account of gastric upset.

Results

The results were assessed in four grades: grade 1, full remission; grade 2, major response; grade 3, minor improvement; grade 4, no improvement.

A full remission in rheumatoid arthritis is defined as a state of excellent general health without any joint complaint, normal E.S.R., normal blood count, and being able to lead an active, unrestricted life. Major response (grade 2) comprises a group of patients who had greatly benefited by chloroquine treatment, but who still had minor handicaps—for instance, limited range of movement of a single joint or incapacity to walk beyond 3 miles (5 km.). The few patients who had improved slightly but remained considerably handicapped in their daily lives were placed into grade 3. Grade 4 is self-explanatory.

In 12 patients a full remission was obtained, with weight gain and return of E.S.R. to normal. A major response (grade 2) was observed in 19 patients who take salicylates from time to time but are leading active lives. Minor improvements occurred in four patients and four failed to benefit at all. About 80% of our cases derived a full remission or major benefit by treatment with chloroquine. The failures (grades 3 and 4) include patients with active rheumatoid arthritis of many years' duration as well as patients with quite recent development of joint lesions. On the other hand, some of the best results occurred in long-standing cases (eight years' and five years' history of rheumatoid arthritis in two of our series). Secondary degenerative joint changes with irregularities of joint surface and narrowing of joint spaces remained unaffected, but remineralization of osteoporotic bones took place under treatment. We have not observed relapses in patients after an initial response to chloroquine and whilst taking not less than 400 mg. daily. Bagnall recorded 18 relapses (less than 1.5% of his series). The difference between our results and those of Bagnall may be explained by the different dosage employed. The therapeutic dose given by us was 450 mg.

of chloroquine alkaloid, whereas Bagnall prescribed only 150 mg. base. Our maintenance dose was 300 mg. base daily.

Discussion

If antimalarial drugs, chloroquine in particular, have a beneficial effect on the disease process of rheumatoid arthritis, the question of its mode of action arises. Haydu investigated the effects of chloroquine as an adenosine triphosphatase inhibitor in rheumatoid arthritis. He regarded the high tissue requirements for adenosine triphosphate and the lack of corticoid support—for example, during infection and mental stress—in certain constitutional types as the basis of rheumatoid arthritis. Kurnick (1956) found that chloroquine combined with desoxyribonucleic acid and thereby prevented its depolymerization. This breakdown of the molecule is the preliminary to sequestration of the nuclear material and to phagocytosis, which represent the L.E.-cell phenomena. In other words, the addition of chloroquine *in vitro* to a system otherwise positive for the L.E.-cell phenomena will prevent the reaction taking place.

Experience gained in treating and following up 39 patients suffering from rheumatoid arthritis up to four years does not justify sweeping statements about the effect of a new drug. It was our original intention to publish a five-year review of our observations, but the recent interest aroused in chloroquine as a potentially useful drug in the management of rheumatoid arthritis has induced us to publish this report.

The assessment of any new treatment of rheumatoid arthritis is not easy, as remissions—some of them permanent—may occur at almost any stage of the disease. It is unlikely, however, that anyone experienced in the management of rheumatoid arthritis would attribute a maintained state of remission in over two-thirds of cases under observation to the natural course of the disease. The *Lancet* (1958) dealt with prognosis in rheumatoid arthritis based on observations in the Rheumatic Unit in Edinburgh between 1948 and 1951. 43% of cases admitted in the first year of illness but only 10% of those admitted between the fifth and tenth years were free from any restriction in activity six years later. Hospital treatment comprised bed rest, plaster splints, salicylates, and physiotherapy. These "sound and uncontroversial methods" and ancillary measures (induced pyrexia and transfusions) have in the past failed to bring an arrest of the condition in the majority of cases. The best results have been achieved by long-continued chrysotherapy, using small weekly doses. Gold failed, however, quite frequently even in cases with a short history of illness. Chloroquine does not seem to distinguish between old and recent cases so long as the disease process is active. We have given up corticosteroids for systemic treatment of rheumatoid arthritis altogether and use them only as hydrocortisone acetate for local injections into single joints to achieve mobility and overcome contractures during the first few weeks, until chloroquine takes effect.

It is too early yet to know how patients with rheumatoid arthritis treated with chloroquine will fare after five to ten years. Long-term maintenance treatment with chloroquine has been planned for the patients under review until the day when the enigma of rheumatoid arthritis has been solved and a more specific and radical cure has been discovered.

In the meantime, we believe that further trials of chloroquine in the treatment of rheumatoid arthritis are justifiable in view of the results achieved so far and the lack of dangerous side-effects of the drug.

Summary

The literature on the use of chloroquine in the management of rheumatoid arthritis is reviewed.

Results in treatment and following up 39 patients from three months to four years are described.

Complete remission of the disease process was obtained in 30% of cases, a major improvement occurred in 50%, and insignificant or no benefit was noted in about 20% of the patients.

The drug proved harmless and was well tolerated in larger doses than used by other authors. Relapses whilst on chloroquine were not observed in our series.

We recommend a regime of treatment consisting in bed rest, induced pyrexia, blood transfusions, and salicylates during the first three weeks of treatment, and tablets of chloroquine sulphate, 200 mg. t.d.s., throughout the treatment or immediately after induced fever—this dose of chloroquine to be continued until a remission has been obtained, when the dose may be decreased to 400 mg. daily (equals 300 mg. base). The maintenance therapy may be required for 12 months or longer.

REFERENCES

Bagnall, A. W. (1957). *Canad. med. Ass. J.*, **77**, 182.
Escarpenter-Oriol, J., Carreras Bayés, A., and Sariols Gomez, M. (1955). *Medizinische*, p. 1083. Quoted by Bagnall (1957).
Forestier, J., and Certonciny, A. (1954). *Rev. Rhum.*, **21**, 395.
Freedman, A. (1956). *Ann. rheum. Dis.*, **15**, 251.
Fuld, H. (1958). *Rheumatism*, **14**, 1, 12.
Haydu, G. G. (1953). *Amer. J. med. Sci.*, **225**, 71.
Kurnick, N. B (1956). *A.M.A. Arch. intern. Med.*, **97**, 562.
Lacapère, J., Monier, H., and Vial, G. (1954). *Rev. Rhum.*, **21**, 389.
Lancet, 1958, **1**, 894.
Page, F. (1951). *Lancet*, **2**, 755.
Rinehart, R. E. (1955). *Northw. Med. (Seattle)*, **54**, 713.
—— Rosenbaum, E. E., and Hopkins, C. E. (1957). Ibid., **56**, 703.
Scherbel, A. L., Schuchter, S. L., and Harrison, J. W. (1957). *Cleveland clin. Quart.*, **24**, 98.
—— Harrison, J. W., and Atdjian, M. (1958). Ibid., **25**, 95.

UNCONTROLLABLE POST-OPERATIVE HAEMORRHAGE AFTER INCOMPATIBLE BLOOD TRANSFUSION

BY

JAMES M. MOORE, F.R.C.S.Ed., F.R.F.P.S.

Senior Registrar, Hairmyres Hospital, East Kilbride

It has often been reported that a defect of coagulation may occur in obstetrical conditions and in pulmonary and prostatic surgery. For example, it has been noted in accidental haemorrhage, amniotic fluid embolism, intrauterine foetal death, and missed abortion (De Lee, 1901; Dieckmann, 1936; Moloney *et al.*, 1949; Schneider, 1951; Reid *et al.*, 1953; Barry *et al.*, 1955), following pulmonary lobectomy (Soulier *et al.*, 1952), and in metastatic carcinoma of the prostate (Tagnon *et al.*, 1952; Swan *et al.*, 1957). One of the features of these cases has been hypofibrinogenaemia.

That abnormal bleeding may occur as a transfusion reaction is not so well known, although it has been recorded by American authors on a number of occasions since it was mentioned by Drinker and Brittingham (1919). Muirhead (1951) found nine cases, while Friesen *et al.* (1952) investigated 11. Other examples are given by Wiener (1954) and Stefanini and Dameshek (1955). Krevans *et al.* (1957) studied two instances, and in a survey of the literature found 11 additional reports. No report of a case has been traced in British literature, although Mollison (1956) refers to the condition.

It is the object of this paper to give a clinical account of such a case which had a fatal termination.

Case Report

The patient was a single woman aged 25 suffering from a chronic gastric ulcer. In the past she had undergone appendicectomy and tonsillectomy, and no excessive bleeding had been noted. Menstrual blood loss had been normal. There was no history suggestive of any allergic upset.

Operation.—A Billroth I partial gastrectomy was carried out, and it was uneventful. The anaesthetic consisted of

thiopentone sodium, tubocurarine chloride, gallamine triethiodide, and nitrous oxide, and a pint (540 ml.) of carefully matched homologous group O rhesus-negative blood was given. The operation was completed at 12 noon.

A second bottle of blood was started at 12.30 p.m. When examined 15 minutes later the patient was rather pale, with a slight cyanotic tinge, and there was a little staining from a stab drainage wound. There was little change during the next two hours. At 2.45 p.m., when about two-thirds of the second bottle of blood (360 ml.) had been given, it was discovered that it was in fact group A rhesus-positive blood which had inadvertently been transfused. Immediately, carefully matched blood of the correct group was substituted and 1 pint (540 ml.) of 50% dextrose given in an attempt to minimize renal complications.

At 4 p.m. it was noted that venous blood sent for further cross-matching would not clot, and by then there was considerable fresh bleeding from the stab wound. Only a small amount of altered blood had been aspirated from the gastric tube during the afternoon, but at 6 p.m. there was 15 oz. (450 ml.) of fresh blood and the main wound had started to ooze. The patient became weaker despite continued transfusion, and another laparotomy was carried out at 7.45 p.m.

Second Operation.—About 4 pints (2 litres) of blood was found in the peritoneal cavity with a few clots. There was a general ooze from many areas involved in the previous operation. On opening the stomach more blood escaped, but again this arose from numerous areas, many not at the suture lines. Despite all attempts at haemostasis the ooze continued. The supply of matched blood for transfusion was temporarily exhausted during the operation, and 2 pints (1 litre) of 6% dextran in saline ("dextraven" and "intradex") was given. As nothing further of benefit could be done, the stomach opening was repaired and the abdomen closed with two drainage tubes.

It was now obvious that the patient had developed an abnormal haemorrhagic tendency.

Treatment.—4 ml. of "adrenoxyl" (1.5 mg. of adrenochrome monosemicarbazone dihydrate) and 100 mg. of vitamin K analogue ("synkavit") were given intramuscularly. 10 ml. of 10% calcium gluconate was given intravenously and a rapid transfusion of matched group O rhesus-negative blood continued. After consultation with the director of the regional transfusion centre at 10 p.m. the patient was given 4 pints (2 litres) of fresh dried plasma alternating with blood, and 2 g. of concentrated fibrinogen fraction. At this stage there appeared to be a slight temporary decrease in the rate of blood loss. Fresh frozen plasma was requested for her, but her condition deteriorated and she died at 1.45 a.m. on the day following operation, before it could be given.

She had received a total of 17 pints (9 litres) of blood, 3 pints (1.5 litres) of processed plasma, and 2 pints (1 litre) of dextran, as well as the 4 pints (2 litres) of fresh dried plasma and fibrinogen mentioned above. In all, this represents the administration of approximately 20 g. of fibrinogen, of which half had been given after the haemorrhagic defect had been recognized. In spite of this, up to the time of death, bleeding continued from the drainage tubes in the abdomen and from the gastric tube.

Relevant Post-mortem Findings

There was a large amount of blood and clot in the peritoneal cavity. The stomach was filled with a well-formed clot equivalent to about a pint (0.5 litre) of blood. No open vessels were identified, but there appeared to have been diffuse haemorrhage from the gastric mucosa, in which there were numerous slit-like defects several millimetres in length apparently communicating with submucosal haematomata. The liver and spleen were normal. Histological examination of kidney showed amorphous eosinophilic material, and desquamated epithelial cells in a few convoluted tubules. The lungs appeared oedematous, but there were no histological changes, and selective staining showed no significant intravascular deposits of fibrin.

Blood Examination.—A specimen of venous blood taken at 3.30 p.m. on the day of operation failed to clot in 24 hours, even after the addition of thrombin in excess, indicating afibrinogenaemia. Marked haemoglobinaemia was noted soon after withdrawal, proving rapid destruction of the incompatible blood. A similar specimen taken two days before operation clotted normally.

Investigations at the regional transfusion centre confirmed that the patient was group O, rhesus negative, and that she had received group A blood, which had been rapidly destroyed. The pre-transfusion serum of the patient contained an anti-A haemolysin, and it was considered that this was responsible for the rapid haemolysis of the incompatible cells.

Discussion

The patient undoubtedly developed a haemorrhagic defect associated with afibrinogenaemia. The development of hypofibrinogenaemia has been described by Stefanini and Dameshek (1955). Among the conditions mentioned as leading to the syndrome are haemorrhagic shock and haemolytic transfusion reactions. The patient's condition was good immediately after operation, which had not been associated with significant loss of blood. Therefore, even if haemorrhagic shock can produce such a syndrome, it seems unlikely that it was initially responsible for the onset of the fibrinogen deficiency in this case. The trigger mechanism was almost certainly the transfusion of blood of the wrong group.

Acquired hypofibrinogenaemia might theoretically result from (*a*) defective formation of fibrinogen; (*b*) intravascular clotting following the entrance of thromboplastic material into the circulation, with consumption of fibrinogen; or (*c*) depletion of fibrinogen by fibrinolytic or proteolytic enzymes in the blood. In this case it is unlikely that there was any defect in the formation of fibrinogen, as there was no evidence of impaired liver function. It is possible that intravascular clotting was the cause of the haemorrhagic state, because Quick *et al.* (1954) have demonstrated the thromboplastin-like activity of lysed red blood cells. However, there was no evidence histologically of abnormal fibrin deposition in tissues; nevertheless a fibrin deposit could have been destroyed by fibrinolytic enzymes, the presence of which has been reported in some cases of this syndrome.

The response to treatment was disappointing although there was post-mortem evidence of clotting. Stefanini and Damashek (1955) suggested that the average amount of fibrinogen required in treatment was 2–4 g., but mentioned that 8–20 g. might be necessary. Barry *et al.* (1955) recommended 2–6 g. of the fibrinogen fraction in the treatment of hypofibrinogenaemia of pregnancy, but if this was not available found triple- or quadruple-strength raw plasma equally effective (1 pint (0.5 litre) of the latter strength yielding 4.4 g. of fibrinogen). In this case approximately 10 g. of fibrinogen was given after the haemorrhagic defect had been recognized, but it is possible that this amount might have produced a greater effect if more of the fibrinogen had been in a concentrated form and had been administered over a shorter period. However, the failure of the patient to respond suggests that there may well have been additional factors involved.

Other coagulation elements may have been absent or diminished—for example, prothrombin, Factor V, and platelets (Greenwalt and Triantaphyllopoulos, 1954). Krevens *et al.* (1957) studied two patients after 500 ml. of incompatible blood and in both found hypofibrinogenaemia, hypoprothrombinaemia, and thrombocytopenia, with reduction of Factor V activity in one. (Incidentally, they could find no evidence of increased fibrinolytic activity, and favoured intravascular coagulation as a probable cause of these changes.) In treatment they advised fresh whole blood supplemented by fibrinogen. It may be that the fresh frozen plasma, containing some of these factors, would have been of benefit.

Two pints (1 litre) of dextran 6% in saline was given when matched blood and plasma were temporarily unavailable. In retrospect it is clear that this was inadvisable, as a number of reports have incriminated dextran as a cause of a haemorrhagic tendency (Carbone *et al.*, 1954; Scott, 1955; McKenzie and Langlands, 1956). The mechanism of the process is not clear, and suggestions made include interaction of dextran with fibrinogen, haemodilution, production of thrombocytopenia, and prolongation of the bleeding-time. The patient, of course, had developed abnormal bleeding before the dextran was given, but it is possible that the dextran aggravated the haemorrhagic tendency.

Friesen *et al.* (1952) described similar cases in which post-operative bleeding occurred as a result of a haemolytic transfusion reaction, when over 250 ml. of incompatible blood had been given. They felt that fibrinolysis was an important factor, but considered that a "heparinoid disturbance" was present. Toluidine-blue dye, given intravenously to two patients in a dosage of 15 mg. per kg. of body weight, apparently corrected the bleeding tendency. Such treatment might be worthy of a trial in any refractory case.

Treatment with corticotrophin (200 units intramuscularly) or cortisone (400 mg. intravenously) has been recommended, in addition to fibrinogen, by Stefanini and Dameshek (1955).

If the possibility of a bleeding state after incompatible transfusion had been known, the second laparotomy would probably not have been carried out, and appropriate treatment might have been started earlier.

Summary and Conclusions

A case is described in which there was fatal post-operative bleeding, associated with afibrinogenaemia, following a haemolytic transfusion reaction.

Treatment is discussed, and the following points may be of value in controlling such a condition: (1) early recognition of the fact that a haemorrhagic state has developed; (2) administration of large amounts of the fibrinogen fraction—for example, 2–6 g., repeated if necessary—or the use of quadruple-strength reconstituted raw dried plasma if fibrinogen is not available; (3) fresh frozen plasma, or fresh blood, if there is a poor response to adequate fibrinogen; (4) avoidance of dextran; (5) corticotrophin, cortisone, or toluidine-blue dye intravenously, if not responding.

I am grateful to Dr. John Wallace, the director of the West of Scotland Regional Transfusion Centre, and Dr. A. S. Douglas for their assistance and advice. I should like to thank Mr. K. I. Macrossan for permission to publish details of this case.

References

Barry, A. P., Geoghegan, F., and Shea, S. M. (1955). *Brit. med. J.*, **2**, 287.
Carbone, J. V., Furth, F. W., Scott, R., jun., and Crosby, W. H. (1954). *Proc. Soc. exp. Biol. (N.Y.)*, **85**, 101.
De Lee, J. B. (1901). *Amer. J. Obstet. Dis. Wom.*, **44**, 785.
Dieckmann, W. J. (1936). *Amer. J. Obstet. Gynec.*, **31**, 734.
Drinker, C. K., and Brittingham, H. H. (1919). *Arch. intern. Med.*, **23**, 133.
Friesen, S. R., Harsha, W. N., and McCroskey, C. H. (1952). *Surgery*, **32**, 620.
Greenwalt, T. J., and Triantaphyllopoulos, D. C. (1954). *Amer. J. clin. Path.*, **24**, 1246.
Krevans, J. R., Jackson, D. P., Conley, C. L., and Hartmann, R. C. (1957). *Blood*, **12**, 834.
McKenzie, J. M., and Langlands, A. C. (1956). *Scot. med. J.*, **1**, 323.
Mollison, P. L. (1956). *Blood Transfusion in Clinical Medicine*, 2nd ed., p. 367. Blackwell Scientific Publ., Oxford.
Moloney, W. C., Egan, W. J., and Gorman, A. J. (1949). *New Engl. J. Med.*, **240**, 596.
Muirhead, E. E. (1951). *Surg. Gynec. Obstet.*, **92**, 734.
Quick, A. J., Georgatsos, J. G., and Hussey, C. V. (1954). *Amer. J. med. Sci.*, **228**, 207.
Reid, D. E., Weiner, A. E., and Roby, C. C. (1953). *Amer. J. Obstet. Gynec.*, **66**, 465.
Schneider, C. L. (1951). *Surg. Gynec. Obstet.*, **92**, 27.
Scott, J. S. (1955). *Brit. med. J.*, **2**, 290.
Soulier, J. P., Mathey, J., Bolloch, A. G. Le. Daumet, Ph., and Fayet, H. (1952). *Rev. Hémat.*, **7**, 30.
Stefanini, M., and Dameshek, W. (1955). *The Hemorrhagic Disorders*, pp. 190, 214. Grune and Stratton, New York and London.
Swan, H. T., Wood, K. F., and Daniel, O. (1957). *Brit. med. J.*, **1**, 495.
Tagnon, H. J., Schulman, P., Whitmore, W. F., and Kravitz, S. C. (1952). *J. clin. Invest.*, **31**, 666.
Wiener, A. S. (1954). *N.Y. St. J. Med.*, **54**, 3071.

THE ISOLATION OF TRYPANOSOMA RHODESIENSE FROM A BUSHBUCK

BY

R. B. HEISCH, M.D.

J. P. McMAHON, O.B.E.

AND

P. E. C. MANSON-BAHR, M.D., M.R.C.P.

From the Division of Insect-borne Diseases, Medical Research Laboratory, Kenya

It has long been believed that an animal reservoir of Rhodesian sleeping sickness exists, but only one serious attempt has been made to isolate polymorphic trypanosomes from game animals and to test their pathogenicity in man. This was done recently by Ashcroft (1958), who killed 74 animals of various species in two endemic areas in Tanganyika and inoculated blood from them into rats. One polymorphic strain was isolated from a Coke's hartebeest (*Alcelaphus cokei*) near Babati in the Mbulu District and inoculated into man with negative results; this strain was presumably *Trypanosoma brucei*. It must be stressed that the only sure way of differentiating *T. rhodesiense* from *T. brucei* is by the inoculation of man. *T. rhodesiense* infects man while *T. brucei* does not: both trypanosomes are morphologically identical.

The present experiment was carried out on Utonga Ridge, a small peninsula projecting into Lake Victoria about 40 miles west of Kisumu in the Nyanza Province of Kenya. This area was chosen because not only were a few natives suffering from Rhodesian sleeping sickness found near by but because *T. rhodesiense* had been isolated from *Glossina pallidipes*, which is now the predominant tsetse fly on the ridge. Between April and August, 1958, 24 animals, which included 13 duikers, 10 bushbucks, and one serval cat were shot and their blood inoculated into rats. The serval cat was negative, but a strain of polymorphic trypanosomes and *T. congolense* were isolated from the duiker, and two polymorphic strains and two strains of *T. congolense* from the bushbuck. The polymorphic strains were inoculated into human volunteers and one of those from the bushbuck (*Tragelaphus scriptus* Fall.) was pathogenic to man (see below). This strain, which is highly pathogenic to rats and produced numerous posteronuclear forms, is presumably *T. rhodesiense*. This is the first time that *T. rhodesiense* has been isolated from animals and establishes finally that Rhodesian sleeping sickness is a zoonosis.

The bushbuck strain was inoculated into the forearm of Mr. C. A. W. Guggisberg, mammalogist on our staff. The inoculum was heavily infected and consisted of 25 ml. of blood from a subinoculated rat with numerous trypanosomes in its blood (over 100 per oil-immersion field). On the seventh day there was a hardish lump at the site of the inoculation and trypanosomes were seen in material aspirated from the swelling. On the eighth day scanty trypanosomes appeared in the blood and the temperature rose to 103° F. (39.4° C.). On the ninth day the arm was very swollen, with a hard inflamed area about 3 in. (7.5 cm.) in diameter on which was a blister about the size of a half-crown. Fluid from the blister contained about three trypanosomes per oil-immersion field. At 11 p.m. the temperature rose to 106.9° F. (41.6° C.) and the patient felt very ill. At 11.45 a.m. he was given his first injection of antrypol. Response to treatment was dramatic and recovery uneventful. Rats inoculated on the ninth day with exudate from the blister and blood taken from an earlobe became infected.

The technique employed is considered of great importance. It is essential to inoculate enough blood (30 ml. at

least) from the animal killed into enough rats (six at least), otherwise light infections can easily be missed. In our opinion Ashcroft inoculated too little blood into too few rats; this may be the reason why he isolated so few strains from such a comparatively large sample of animals. Experiments of this kind must be designed with a broad sweep on a large scale and may have to be continued for a considerable time.

Although the isolation of *T. rhodesiense* from a bushbuck is important, it would be interesting to repeat the experiment in areas where *G. morsitans* and *G. swynnertoni* are vectors of sleeping sickness to discover whether the same or other species of animals are acting as reservoirs. This note gives only a brief account of our work; detailed results will be published elsewhere.

We are much indebted to Messrs. Harvey, Harmer, and Highton for their enthusiastic work in the laboratory and the field.

REFERENCE

Ashcroft, M. T. (1958). *Trans. roy. Soc. trop. Med. Hyg.*, **52**, 276.

SECOND BACTERIOLOGICAL STUDY FROM A MATERNITY HOSPITAL

BY

FRANK MARSH, M.D., D.T.M.&H.

Director of Pathology, Epping Hospitals Group

The measures used in a maternity hospital to check the growth and build-up of pathogenic micro-organisms in lying-in wards and nurseries have already been described (Marsh and Rodway, 1954). That paper covered a period of some 38 months, and the methods used were described in some detail. The present paper extends the study for a further four years—to nearly eight years in all.

Floors were treated with "marinol D." After the discharge of a patient, disinfection of a ward was effected by spraying chlorhexidine 1:5,000 from a "microsol" disperser. Blankets were washed in "lissapol N" (1:200) and disinfected with "fixanol C" (1:200). For a while "cirrasol O D" was used, but fixanol C was preferred. Blankets of the mothers were treated every two to three weeks; blankets of the babies every 10 days. Mattress sterilization was by Sparkhall, each time a new occupant used the bed. The rubber or sorbo mattresses of the infants were treated by wiping with a dilute solution of "dettol," "roccal," or chlorhexidine. The pillows were at first disinfected with formalin, but later this treatment was abandoned and plastic covers were used for the pillows. Since May, 1955, hand cream has been supplied for the nursing staff and also for the mothers, after they had washed their hands. Chlorhexidine and roccal were incorporated in the hand cream, 50% of each; the two compounds seemed to be equally effective.

Results

Records were kept of 211 blood-agar plates exposed in the wards during periods of activity. No colonies of *Staphylococcus aureus* were observed. Numerous colonies of *Staphylococcus albus* were identified. On two occasions a few colonies of *Streptococcus haemolyticus* (Lancefield group A) were found on a plate. A total of 477 swabs (nasal 243, eyes 165, and umbilical 69) from infants were examined. *Staph. aureus* was isolated from 58.8% of nasal, 48.4% of eye, and 55% of umbilical swabs taken between the eighth and the tenth days of life. (Penicillin-resistant staphylococci were found in 75 to 90% of the earlier (pre-1954) series, and in 65 to 80% of the present series (1955–7). Infection among 4,919 infants (1955–7) was 2.5% (respiratory infections 0.2%, minor skin lesions 1.3%, eye infections 0.18%).)

A total of 309 swabs from mothers were examined (110 nasal, 124 throat, and 75 nipple). *Staph. aureus* was isolated from 23.6% of nasal, 6.5% of throat, and 47.9% of nipple swabs. (*Staph. aureus* was insensitive to penicillin in 75% positive swabs in 1955, and in 65% positive swabs in 1957.) From January, 1950, to December, 1953, among 4,830 patients (including 64 admitted after delivery) there were 5.3% puerperal pyrexia cases. In 1953 three cases of breast abscess occurred; there were none in 1955–7. (A few postnatal women—a week or two after discharge—developed a breast abscess.) A total of 310 swabs from nursing staff were examined (150 nasal, 111 throat, and 49 hand). *Staph. aureus* was found in 34% of nasal, 4.5% of throat swabs, and in one hand swab. Of these strains 90% were resistant to penicillin.

During the second four-year period, 22 midwives and nurses and 202 pupil midwives were employed. Infections occurred in 75 individuals (33.6%). Four-fifths were minor respiratory cases, mainly tonsillitis and influenza. Other cases included minor skin lesions, boils, and furuncle of the ear (3.5%), eye infections (styes) 1.8%, gastro-enteritis 0.27%, and one case of glandular fever. *Staph. aureus* was not isolated from exposed plates—that is, from air-borne settles—but the micrococcus was isolated from the nasal, eye, and umbilical swabs. Of 255 neonatal deaths, respiratory infection was found in 2.3%.

The methods evolved for the prevention of cross-infection show some success; but *Staph. aureus* implanted in the noses of infants did not seem to be unfavourably affected.

It is thought that *Staph. aureus* confined to the noses of infants may not be harmful unless some means of dissemination occurs.

I thank Miss Helen Rodway, consultant obstetrician, Thorpe Coombe Maternity Hospital, London, for collecting the data and for enlightened supervision of the fight against cross-infection; and Dr. H. Caplin, director of pathology, Forest Hospitals Group, for undertaking many of the swab examinations.

REFERENCE

Marsh, F., and Rodway, H. E. (1954). *Lancet*, **1**, 125.

Medical Memorandum

Acute Haemolytic Anaemia in a Case of Infantile Gastro-enteritis Treated with Oxytetracycline

Anaemia of mild or moderate degree following infantile gastro-enteritis is not uncommon, and is usually thought to be due to a toxic depression of blood formation, often in association with a nutritional deficiency. It is not known whether haemolysis plays any significant part. By infantile gastro-enteritis we mean a specific disease due to a number of serologically distinct types of *Escherichia coli*: an acute severe haemolytic anaemia following this condition has not been seen before in this unit. The following case is reported because other workers may have had similar experience and may be able to shed further light on its aetiology.

CASE REPORT

A male infant aged 6 months was admitted to hospital on December 5, 1956, with a five-day history of diarrhoea with some vomiting. His temperature was 98° F. (36.7° C.), pulse 134, and respirations 32. He was an ill child, with moderate dehydration and sore buttocks, but otherwise clinical examination was negative. He had not had any previous illness and there was nothing relevant in the family history. Glucose saline (2.5% glucose in 0.3% sodium chloride) was given by mouth, and after two specimens of

faeces had been obtained oxytetracycline, 50 mg. six-hourly, was begun. After 24 hours his condition had much improved and there was no dehydration. Subsequent progress was uneventful, and oxytetracycline was discontinued on December 11 after a five-day course. At that time he appeared very well, the stools were normal, and the feeds had been increased to full-cream National dried milk.

On December 5 and 6 a pure culture of a smooth type of *E. coli* was isolated from the faeces. It was, however, an anaerogenic strain and was not typable with our sera (O26, O55, O86, O111, O114, O119, O125, O126, O127, and

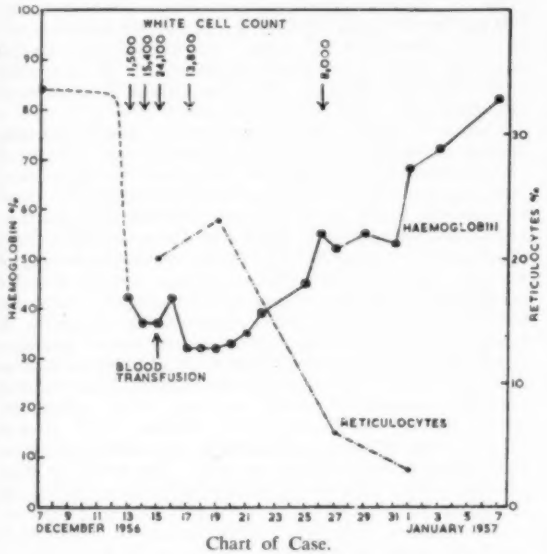


Chart of Case.

O128 sera are used routinely). On December 12 only rough *E. coli* were isolated. The haemoglobin on December 7 was 12.6 g./100 ml. (85% Haldane); the Chart shows the further levels.

On December 12 the child was noted to be rather pale; his temperature was 99° F. (37.2° C.). Next day the pallor was marked and there was a subconjunctival haemorrhage in the right eye. The sclerotics showed a suspicion of icterus. He became progressively more ill and on the 15th there was marked air hunger. A small transfusion of about 200 ml. of compatible group A Rh-negative blood was given. The haemoglobin rose slightly on the 16th, but fell again next day. From December 22 there was a steady rise in the haemoglobin value. From December 12 to 22 the bone marrow was very active, but was only able to maintain the haemoglobin at a constant level. The circulating red cells showed an astonishing degree of anisocytosis. Many macrocytic cells were present together with about 5% normoblasts and a maximum reticulocytosis of 23%. The white-cell count increased, reaching a peak of 24,100/c.mm. with many myelocytes and metamyelocytes.

On December 14 the serum bilirubin was 1.3 mg./100 ml. and the liver-function tests were normal. Next day the direct Coombs test was negative on two specimens of blood. On the 19th the test for occult blood in the faeces was negative. The faecal stercobilinogen content was 130 mg./100 g. of moist stool; this figure was thought to be too low for a patient suffering from haemolytic anaemia until it was realized that in an infant's stool most of the pigment was likely to be in the form of bilirubin. There was insufficient material for a quantitative assay of bilirubin in the stool, but qualitative tests showed a very large quantity to be present. On December 21 the faecal stercobilinogen content was less than 20 mg./100 g. of moist stool; bilirubin amounted to 400 mg./100 g. of moist stool. A week later the bilirubin content was 250 mg./100 g., and the stercobilinogen content 10 mg./100 g. of moist stool. Assays of the bilirubin and stercobilinogen contents of the stools from two infants of the same age who had just recovered from infantile gastro-enteritis showed 50 mg. and 110 mg. of bilirubin and 15 mg. of stercobilinogen per 100 g. of moist stool. The levels found in the patient were obviously greatly in excess of these, indicating that the anaemia was haemolytic in origin.

Red-cell fragility on two occasions was normal. During the period of acute anaemia there was no recurrence of diarrhoea. The stools were of an orange colour, and this was clearly due to the large amount of unaltered bilirubin present. The reduction of bilirubin to stercobilinogen may be imperfect in infants, and the removal of the normal flora by the action of oxytetracycline undoubtedly slowed down the process. Repeated stool examinations did not show any pathogenic organisms. Apart from the small blood transfusion mentioned, no other treatment was given except for several injections of vitamin B_{12} on the basis that a great deal of blood regeneration was necessary to compete with the haemolysis that was occurring. Between December 11 and 17 there was pyrexia of 99 to 101° F. (37.2 to 38.3° C.), but from the 17th onwards he remained afebrile.

From December 22, when the haemoglobin rose steadily, there were no setbacks, apart from a cross-infection with *E. coli* type O127 which led to a mild gastro-enteritis on January 3, 1957. The blood count was unaffected, but on this occasion the patient was treated with neomycin. By January 7 the haemoglobin had risen to 12.3 g./100 ml. (83% Haldane) and the red cells appeared normal. Follow-up on February 12 showed exactly the same figures.

Comment

From the history and clinical examination the case appeared to be one of infantile gastro-enteritis. A smooth *E. coli* was isolated from the stool which was not a recognized pathogenic type, but which might nevertheless have been a pathogenic strain. This has occurred not infrequently, and some strains have been identified by Dr. Joan Taylor, at Colindale, as identical with those causing gastro-enteritis from other areas.

A severe haemolytic anaemia developed about 10 days after the onset of the illness. Haemolysis continued, and in spite of a very active marrow no rise in haemoglobin was recorded for about 10 days. The red-cell fragility was normal and no circulating antibody was demonstrated by the Coombs test. The nature of the haemolysin remains unknown. At the time of onset of the haemolytic anaemia the child appeared to have recovered from gastro-enteritis and there was nothing to suggest a source for the circulating toxin.

The acute haemolysis occurred after a course of oxytetracycline. Thrombocytopenic purpura following this antibiotic has been described by Welch *et al.* (1954) and Beckett *et al.* (1955). The former mention the occurrence of other blood dyscrasias, but make no direct reference to haemolytic anaemia. A search of the literature has not revealed a previous case; nevertheless, oxytetracycline remains a possible cause.

Cross-infection later with another known pathogenic type of *E. coli* (O127) led to a mild gastro-enteritis on January 3, but the blood count was unaffected. This infection was treated successfully with neomycin. Subsequent follow-up has not shown any abnormality in the blood picture.

E. H. BROWN, D.M., M.R.C.P., D.C.H.,
Assistant Physician, Hither Green Hospital, London.
E. H. BAILEY, M.R.C.S.,
Pathologist, Southern Group Laboratory.

References

Beckett, A. G., and Foxell, A. W. H. (1955). *Lancet*, **1**, 1053.
Welch, H., Lewis, C. N., and Kerlan, I. (1954). *Antibiot. and Chemother.*, **4**, 607.

Reviews

SOCIAL WELFARE IN SCOTLAND

Scottish Social Welfare, 1864–1914. By Thomas Ferguson. (Pp. 609+xi; illustrated. 42s.) Edinburgh and London: E. and S. Livingstone Ltd. 1958.

This account, by Professor Ferguson, of the Scottish social welfare services is comprehensive and well documented. It is full of facts and figures supported by apt quotations. The 50 years covered show the evolution from primitive conditions to the beginnings of the Welfare State. Though the book is long, it is a pity that it stops at 1914, and it is to be hoped that a further volume, to bring it up to date, is contemplated.

The early chapters describe in considerable detail the housing, earnings, diet, and general environment of the people, ranging from the slum-dwellers of the great cities to the lonely crofters and cottars of the Highlands and Islands living, along with their animals, in "black houses." Then there are over 120 pages on the relief of destitution, and all the controversies about rates of relief and whether any relief should be given to the able-bodied. This is followed by chapters with a greater medical flavour on the infectious diseases, cholera, smallpox, typhus fever, tuberculosis, and certain zoönoses; on the care of the sick, domiciliary and institutional; and on the welfare of mothers and young people.

The half-century saw the beginning of the famous Highlands and Islands Medical Service, and the establishment in 1894 of the Local Government Board, which incorporated the functions of the Board of Supervision and retained for long the latter body's Poor Law outlook with its fixed principle of discouraging idleness and imposture. It saw in 1855 the highest death rate and in 1868 the high-water mark of pauperism. The living conditions described are so degrading as to be almost unbelievable. Quotations show that Professor Matthew Hay, of Aberdeen, wrote that typhus fever was spread by body vermin. This was in 1904, and several years before the role of the louse in this disease was generally accepted.

Scotland is well known for its housing problems, but it is not so well known that at the census of 1871 32.5% of the houses had only one room and that 5% of those living in them consisted of families of ten or more. The reader is brought up against the decline in the purchasing power of money when told that in 1906 the pay for unskilled labourers was 5½d. an hour, and that house rents in the country districts were about £1 to £3 a year.

In a serious book such as this it is a relief to come across a lighter touch, as is the account of the formal opening by Royalty in 1903 of the Colinton Fever Hospital in Edinburgh. The guests arrived early. By inadvertence the doors of the refreshment rooms were opened too soon, and by the time the ceremony was due to start "the tables had been literally swept of all vestige of food."

The book deals not only with purely medical matters, but also with those, now comprised in the term "social medicine," which lead to, or are at least associated with, ill-health. It can be highly recommended, and there is a full bibliography for those who wish to gain even further information.

ALLEN DALEY.

A GREAT MEDICAL EPOCH

The Medical World of the Eighteenth Century. By Lester S. King, M.D. (Pp. 346+xvii; illustrated. 43s. 6d.) Chicago: University of Chicago Press. London: Cambridge University Press. 1958.

The author of this interesting monograph, looking forward as well as backward from the viewpoint of the eighteenth century, finds that a study of this epoch will enable us to understand better "our mature present-day medical structure." He begins his survey by a rather lengthy account of the feud between physicians and apothecaries which exercised so potent an influence upon medical progress, and he seasons his remarks by quoting from Sir Samuel Garth's poem, "The Dispensary." The second chapter deals with "Quack and Empiric," from the common-sense John Wesley and his popular work, *Primitive Physick*, to Sir William Read, the royal oculist in the time of Queen Anne, and from Berkeley's tar-water to Joshua Ward's drop and pill.

As might be expected, considerable space is devoted to Hermann Boerhaave, by far the greatest physician of the eighteenth century, who strove to blend old and new facts and theories into a well-organized system. His theories were "by no means models of lucidity." So the author tells us, but it is disappointing to find that his own attempts to explain Boerhaave's "gluten," "acrimony," and the like leave the reader more mystified than ever. It is a relief to pass from Boerhaave to the more readable description of the eighteenth-century view of fevers.

"Similia Similibus" is the title of a long and illuminating account of Hahnemann and his homoeopathy. The word suggests infinitesimal dosage, but the prescribing of one drug at a time, and the belief that a drug which produced certain symptoms in health would cure disease marked by the same symptoms, were ideas of equal importance in this system, which arose as a reaction against the barbarous therapy of the day. It was during the eighteenth century that the nomenclature of disease was closely studied, under the stimulus of Linnaeus, whose classifications of plants, or taxonomy, was extended to diseases and called nosology. Emphasis is laid upon the pioneer work of François Boissier de Sauvages, the title-page of whose book is reproduced, entitled *Nosologia Methodica* and dated 1768. About this period William Cullen turned his brilliant talent towards nosology, but it was not yet possible to separate symptoms from diseases, and it is not surprising that Benjamin Rush affirmed that "diseases anastomose" and cannot be classified.

Other leading phenomena of the eighteenth century were the development of medical ethics and of the modern outlook in pathology. John Gregory's lectures "On the Duties and Qualifications of a Physician" were followed by Thomas Percival's important work which coined the term "medical ethics" and was the forerunner of all modern ethical codes. In pathology Morgagni's *De Sedibus et Causis Morborum* in 1761 inaugurated a new era, although the forgotten work of Lieutaud also deserves attention. The concluding chapter, which might well have been longer, describes the rise and fall of inoculation against smallpox and the ever changing attitude in medical practice.

This interesting account of a great epoch deserves to be studied and pondered. Sir Robert Sibbald is not Sibbold (pp. 26 and 27), nor was he appointed professor "early in the century," but in 1685. Again, "empire" on page 34 should be "empirics." These, however, are trivial errors. The bibliographic notes on each chapter are of value, and show that the author has been careful to draw his information from the original sources. It is perhaps a pity that so little mention is made of recent books and articles on the same topic. There are an excellent foreword by Professor Ilza Veith and an adequate index.

DOUGLAS GUTHRIE.

REHABILITATION IN THE U.S.A.

The Handicapped and Their Rehabilitation. Edited by Harry A. Pattison, M.D., F.A.C.P. Introduction by Major-General Melvin J. Maas, U.S.M.C.R. ret. (Pp. 944+xxxii; illustrated. £5 12s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957.

This book is a mixture of sermon, encyclopaedia, training manual, and synopsis of medical practice. Forty-four authors contribute, and all save one are from the United States of America. Section I—the sermon—contains full extracts from the writings of leading American authorities on rehabilitation such as Kessler and Rusk. Section II deals with specific handicaps, diseases, and age groups. The American public is more informed medically than most, but

it is difficult to believe that they, and for that matter the trained medical auxiliaries, could follow and understand the significance of the technicalities referred to in Chapter 5. Medical practitioners will, on the other hand, find the chapter most rewarding. Another chapter (Chapter 10), entitled "What is Being Done for the Aged," will be very useful for reference to anyone unfamiliar with the work in this field. The majority of the chapters in this section contain full and sound advice and indicate the scope and the basic principles of rehabilitation, stressing always the needs of the individual. Occasional references to the problems of medical diagnosis as already indicated seem to imply that the book is written for the medical graduate. This confusion as to whom the book is designed for is possibly resolved on page 401, where it is stated: "The responsibility for assisting the physician in charge by co-ordinating the activities of the rehabilitation team and for developing on the staff a rehabilitation consciousness are phases of the work of a new profession in the medical field, whether we call the position Rehabilitation Counsellor, Rehabilitation Co-ordinator or Executive Assistant." Section III is a résumé of the role, and occasionally of the training programme, of the different members of the team, and Section IV deals with American practice. The latter affords an excellent survey of the development of rehabilitation services in the U.S.A., both Federal and State and also in industry. This section will be of value to all interested in rehabilitation problems and procedures. Apart from these aspects, the book is essentially designed for the members of the rehabilitation team in the United States of America and thus has a very limited appeal to readers in Western Europe.

R. E. TUNBRIDGE.

STUDY OF BODILY FUNCTION

Taschenbuch Klinischer Funktionsprüfungen. Edited by Arthur Gitter and Ludwig Heilmeyer. Fifth edition. (Pp. 484+xx; illustrated. DM. 18.) Jena: Gustav Fischer Verlag. 1958.

This handbook on clinical procedures by Dr. A. Gitter and Professor L. Heilmeyer deals with the study of function in various organs and systems. The fact that it has reached its fifth edition within four years is some indication of its popularity and usefulness to the German clinician, although the British reader will be conscious of some confusion between detail and repetition. The aim of this book is to describe those practical procedures which determine minor or major abnormalities of function where these are of diagnostic value.

Experimental methods in clinical medicine at the bedside are becoming increasingly important. Recent advances, particularly during the past decade, in all branches of general medicine demand the closest liaison between laboratory procedures and the basic principles of sound clinical methods—to wit, good history-taking and clinical examination of every system (with particular attention to the system currently involved). An adequate knowledge of basic principles in radiology, applied physiology, and pathology has for some years been included in the armamentarium of the practising clinician. To-day clinical laboratory procedures include applied physiological, biochemical, and haematological disciplines which must all be integrated with clinical medicine and brought to the bedside. Only in this way can the physician assess the value and limitations of such investigations.

In the sphere of thoracic medicine, the applied physiology of respiration with special reference to the mechanics of ventilation, disturbances of gas exchange in blood and alveoli, tests of pulmonary function, and methods of study by spirography and bronchospirometry, and the like; in the cardiovascular system, angiocardiography, cardiac catheterization, and methods of investigation of the arteries by oscillometry and arteriography; and skin and muscle investigations of blood supply, are among many other features outlined. Tests of renal and liver function and those concerned with endocrine and metabolic disorders are all reviewed; in fact, no system is neglected, and some are dealt with in even greater detail than the average reader would consider necessary. There is a very full bibliography, but one could wish that this bibliography had a more international flavour. The book is well produced in a most convenient form, and is, for myself, among the few books I have seen from the presses of East Germany.

PHILIP ELLMAN.

RECTOSCOPIC APPEARANCES

Principles of Rectoscopy. By Karel Herfort and Zdenek Maratka. (Pp. 254; illustrated. 42s.) London: Constable and Co., Ltd. 1958.

The objective of this book, orginally written in Czech but with triple translation into Russian, German, and English contained in the one volume, is to describe the technique of proctoscopy and sigmoidoscopy and to record pictorially certain lesions of the anus, rectum, and colon. The author describes his preferred knee–elbow position for sigmoidoscopy and concerns himself with certain of the difficulties and hazards of the examination, but this section has nothing to add to the routine description of the procedure contained in any monograph devoted to proctology. The volume is copiously illustrated, but without reference to the captions I have found it difficult to recognize some of the lesions portrayed in the colour photographs. Two illustrations show the formation of a perineal colostomy and an artificial anus. But the suggestion that a surgical stoma is well sited when placed in these positions will not find general approval amongst English and American surgeons. The multiple artists' drawings of the sigmoidoscopic appearances in the normal and in the diseased bowel are beautifully prepared, but, as in all such illustrations of endoscopic appearances, they tend to be impressionistic rather than realistic. The beginner in sigmoidoscopic examinations may well find initial difficulty in correlating what he visualizes during instrumentation with appearances represented in these colour drawings, but with additional experience they should provide him with considerable help.

Combined with an adequate practical training in the specialty of proctology and the interpretation of sigmoidoscopic appearances the book can play a part. But coloured illustrations, however beautifully prepared, can never replace the experience gained by the detailed and direct observation of the changes accompanying disease processes affecting the rectum and colon.

STANLEY AYLETT.

A bibliography of the publications of W.H.O. from its inception to the end of 1957 is now available (*Publications of the World Health Organization 1947–1957*; 128 pp., H.M. Stationery Office, 17s. 6d.). It lists all articles published in the *Bulletin of the World Health Organization*, all numbers of the *Monograph Series*, the *Technical Reports Series*, and the *Official Records*, and selected material from the *Chronicle*, the *International Digest of Health Legislation*, the *Epidemiological and Vital Statistics Report*, and the supplements to the *Weekly Epidemiological Record*. Certain occasional publications of W.H.O. are also included. The items are serially numbered and grouped alphabetically under subject headings; author and country indexes are provided. The bibliography is also available in French.

In the sixth edition of his *Forensic Medicine* (London, A. and C. Black, 1957; 30s.) Professor Douglas Kerr has made a general revision of the text and has rewritten the section on the treatment of barbiturate poisoning. Mention is made of the B.M.A. report on the *Recognition of Intoxication*, 1954, but the original memorandum published by the Association in 1927 has been retained in the book as being more suitable for teaching purposes, although a table based on data in the later report has been included to show blood alcohol percentages in relation to amounts of beer or spirits consumed.

The Metabolism of Sulphur Compounds, by Professor Leslie Young and Dr. G. A. Maw (pp. 180; Methuen and Co., Ltd., 16s.), deals with various organic and inorganic compounds of sulphur in higher animals and in micro-organisms. Cysteine, cystine, homocysteine, methionine, and other compounds of especial interest are discussed in detail. Each chapter is followed by an extensive bibliography.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY NOVEMBER 15 1958

ENVIRONMENT AND BLOOD PRESSURE

Environmental factors in the production of chronic disease have recently been given increasing attention. The Pneumoconiosis Research Unit in South Wales has been in the forefront in this work, and its interest has not been restricted to respiratory diseases. Recently workers there have been studying levels of arterial blood pressure in the general population, and W. E. Miall and P. D. Oldham[1] have described a study of samples of the population of the Rhondda Fach, a mining valley, and of the Vale of Glamorgan, an agricultural area. The samples, chosen at random, were assumed to be representative of the general population in these two districts and were used as the index cases (propositi) for inheritance studies in which measurements were also made for all the first-degree relatives living within 25 miles of the centre of each area. These relatives comprise parents, siblings, and children. The measurements were made under standard circumstances by one observer.

The results from the samples have been used for fitting curves relating arterial pressure with age, and these show that there is no material difference in the relationship in the two populations despite their strikingly different environments. In further analyses of environmental factors the data from both districts have accordingly been pooled. Comparisons of the arterial pressure of individuals is not possible without standardizing for age and sex. A system of scoring devised by M. Hamilton and his associates[2] has been followed to allow for these variables so that direct comparisons may be made. In this way a number of environmental factors were shown to have a considerable influence on arterial blood pressure. Occupation, either directly or indirectly through economic factors, appeared to affect pressure. People in light work with less expenditure of energy, higher incomes, and higher standards of living had higher pressures. Heavy manual workers with higher expenditure of energy, lower incomes, and lower living standards had lower pressures. There was a steady trend between these two extremes, the intermediate groups having intermediate pressures. These differences were not due to differences of arm girth or weight. Furthermore, the effects of occupation were most obvious in bachelors and in men over 50 years old. The authors point out that these are the two groups of people who most truly reflect occupational differences in income and energy expenditure.

These observations do not entirely agree with those reported in some other studies. In a survey in Birmingham[3] higher pressures were found in Social Class V than in Social Class I, but no real trend with the physical demands of occupation was noted. In Bergen[4] a study has shown that persons occupied in heavy labour have the highest systolic pressure, while those with independent and responsible positions have the lowest blood pressure. The reasons for these discrepancies are not clear, but it may be noted that in the South Wales survey the blood pressure was taken in the individual's own home after a rest of five to ten minutes. The Birmingham records were made without any previous period of rest. In Bergen each person attended at a centre at a time most convenient to himself. It is therefore not perhaps surprising that the labourer coming straight from his place of work presented a higher systolic blood pressure than the sedentary worker.

An investigation of the effect of family size on blood pressure produced some interesting, and at first sight surprising, results. Pregnancy may provoke the appearance of hypertension in some subjects who develop toxaemia, and in some the rise of blood pressure may persist.[5] Accordingly, it might be expected that multiparous women might have higher pressures than nulliparous women. However, on the contrary, an inverse correlation was found with family size—the larger the family the lower the pressure. A similar trend was reported in the women of the Bergen survey.[4] Even more surprising was the finding in the South Wales survey that family size influenced blood pressure in a similar way in the male. The trend for systolic pressure in men aged 15–50 years is almost as marked as in young females, though it is absent in diastolic pressure measurements. Single men had higher systolic pressures than the married, and the fathers of small families higher than those of large families. The influence of family size eventually becomes less obvious in the elderly.

Speculation on the explanation of these environmental effects is tempting but unlikely to be fruitful without further investigation. The fact that the pressures in both males and females are related to family

[1] Miall, W. E., and Oldham, P. D., *Clin. Sci.*, 1958, **17**, 409.
[2] Hamilton, M., Pickering, G. W., Roberts, J. A. F., and Sowry, G. S. C., *ibid.*, 1954, **13**, 37.
[3] Brown, R. G., McKeown, T., and Whitfield, A. G. W., *Canad. J. Biochem.*, 1957, **35**, 897.
[4] Humerfelt, S., and Wedervang, Fr., *Acta med. scand.*, 1957, **159**, 489.
[5] Chesley, L. C., Annitto, J. E., and Jarvis, D. G., *Amer. J. Obstet. Gynec.*, 1947, **53**, 851.

size suggests that the relationship is probably not a direct physiological effect of pregnancy or lactation. Though women with high pressures may be advised to limit the number of children, this advice is rarely given to hypertensive fathers. The factor which associates high fertility with low blood pressure cannot yet be clearly defined, and several possible explanations come to mind. Clearly, a large family brings financial problems and certainly increases energy expenditure, and in this way may diminish some of the distinctions between the social classes. The findings of this application of epidemiological techniques to the study of hypertension will undoubtedly stimulate much further inquiry.

COMPENSATION FOR INJURY

Workmen's compensation attracts the eye of the public, and undoubtedly press reports of accidents and compensation are widely read by employer and employee. It has often been questioned whether changes in the law have been beneficial to the claimant and have facilitated the task of the doctors concerned with his case. The duties of the certifying surgeon and the medical referee were stated in the Workmen's Compensation Act of 1906, when the previous Acts of 1897 and 1900 were repealed. As time went on further changes were made, and a departmental committee on workmen's compensation issued a report[1] in 1920 (the Holman Gregory report) which influenced the trend of further legislation and practice. In 1946 the National Insurance (Industrial Injuries) Act provided regulations governing the constitution of medical boards and medical appeal tribunals. The appointment of medical assessors in connexion with local appeals tribunals was recognized. One of the consequences of all this is that a group of doctors now deal with these cases and not one or two holding a special and permanent position.

These legal changes may have made the work of the claimant's solicitor easier, but they have merely altered rather than simplified the medical procedure. Sometimes all the claimant's family doctor can do is to provide certification and sedatives—perhaps knowing that the provision of both is necessary but may be harmful—while the medical aspects of the claim pass into the hands of a practitioner or group of practitioners whose main occupation is to prepare reports on medico-legal matters. They obtain specialist opinion from consultants, particularly neurologists, psychiatrists, and orthopaedic surgeons. There is little evidence that the frequent medical examinations are of benefit to the litigant, and many observers consider that they are detrimental to him and misleading to the lawyers. In fact it can be argued that the present system of long-drawn-out negotiation sometimes tends to demoralize patients, helping to induce a traumatic neurosis, and robbing their doctors of all opportunity to prevent the onset of this clinical condition, so well known to the courts.

Emotional reaction after injury has been recognized for many years, and circumstances have provided labels for types, such as railway spine and shell shock. Sir Francis Walshe,[2] discussing the subject recently, has observed that some non-medical factor operates to determine the development of traumatic neurosis. The aetiology of the condition has been considered particularly by Farquhar Buzzard,[3] J. Collie,[4] and L. Brahdy and S. Kahn,[5] as well as Walshe, to name only a few. Their observations show emotional symptoms are more likely to arise after an injury resulting from war or earthquake, or from accidents on the railway or in industry, and particularly in the course of gainful employment, than from injury received on the rugby football ground, hunting field, racecourse, or in childhood. Indeed, traumatic neurosis is rarely found in childhood, though parents suing on behalf of a child may present symptoms of a neurosis. The patient's pretraumatic personality is not necessarily other than normal, but accidents of a particular type or to certain areas of the body are more apt to produce manifestations of traumatic neurosis. If the injury is emotional rather than physical—such as a fright—then headache, fear, vertigo, tremor, and insomnia may develop, though these may also develop after physical injury. Such symptoms are well known after injury to transverse processes of vertebrae, coccyx, head, and neck. In these circumstances it can be difficult to determine if the claimant is a sick man seeking adequate compensation, or a malingerer. Walshe concludes that "trauma by itself does not give rise to neurosis, but when a claim for compensation can be made in respect of an accident or injury, this factor allows, if it does not actively induce, the neurosis. In its absence neurosis does not ensue upon injury." And it is commonly observed that settlement of a patient's claim to his satisfaction usually leads to an improvement or cure, temporary or permanent, of the traumatic neurosis. The remarkable benefit that follows settlement has attracted attention in the courts of many countries. Lump sums have always been popular with the work-

[1] Departmental Committee on Workmen's Compensation, 1920, H.M.S.O., London.
[2] Walshe, F., *Med. Press*, 1958, **239**, 493.
[3] Buzzard, E. F., *Lancet*, 1923, **2**, 1285.
[4] Collie, J., *Fraud in Medico-legal Practice*, 1932, London.
[5] Brahdy, L., and Kahn, S., *Trauma and Disease*, 1937, Philadelphia.
[6] Stewart Report, 1936, quoted by Wilson, A., and Levy, H., *Workmen's Compensation*, 1941, London.

man. Now that treatment is provided by the State this is of less importance, but it is worth noting that they are prohibited in many foreign countries, and evidence[6] from the Ministry of Pensions was that they had not proved successful in cases of war neuroses.

To help the judge decide whether a litigant's condition is legally directly or indirectly the result of injury, the doctor has a duty to state what he finds, and, if asked, he will give his opinion on whether the symptoms result from the injury. Hence it is not for him to decide if there is malingering or fraud, but the doctor can be of great assistance to the court if he can say the man is genuine and he considers him to be as disabled as he claims to be. Walshe draws important conclusions on the enormous loss to industry of the complications, particularly neurosis, after injury, and the distress to the injured person. He points out that the process of negotiation is often not only interminable but of such a nature as to aggravate the emotional condition of the litigant. Are doctors sometimes at fault in writing pessimistic reports? Are lawyers sometimes blind to the advantages for the claimant of an early settlement? In the end the injured person's recovery is likely to mean more to him than any financial award.

LIVE POLIOMYELITIS VACCINE

An Expert Committee[1] of the World Health Organization, reporting earlier this year, had this to say about living attenuated poliomyelitis vaccines: "Tests on hundreds of thousands of people will be necessary to establish whether the theoretical expectations of safety can be confirmed in actual practice." "Tests" of this magnitude are already in progress in different parts of the world, and a preliminary report on one of them, involving 244,596 persons vaccinated in the Belgian Congo and Ruanda-Urundi, has already been published.[2] Three articles in this issue focus attention on "the theoretical expectations of safety" of the living attenuated poliomyelitis vaccines so far available. Professor C. H. Stuart-Harris and his colleagues in Sheffield (p. 1188), using Sabin's attenuated type III polio virus, designated $12a_1b$ (KP_4), in a rigidly controlled trial on 14 boys first immunized with two injections of the formolized vaccine, found that virus isolated from all five of the boys in whose intestines it multiplied regained its power to paralyse monkeys inoculated intracerebrally. Virus isolated from one case on the fourteenth day after ingestion of the vaccine "showed a degree of neurotropism similar to that of field strains of type III virus from paralytic cases." It is unlikely that any of the strains isolated from boys in this trial was a "wild" strain accidentally picked up, because "no case of type III poliomyelitis was in fact encountered in Sheffield during the entire period of the trial, and the last case of type III virus isolation had been in December, 1956." In another article (p. 1187) Dr. D. S. Dane and Professor G. W. A. Dick and their colleagues in Belfast record neutralizing antibody levels in 60 children vaccinated orally a year previously with living attenuated type II TN virus. Their earlier report[3] had shown that this virus regained its cytopathic power and some power to paralyse monkeys in its passage through the human intestine, a result which led to universal agreement[2] that, on grounds of safety, the TN strain is unsuitable as a vaccine. The Belfast workers now show that the level of neutralizing antibody in the same children a year after vaccination is "of the same order as in children a year after vaccination with two injections of formolized vaccine." This result is disappointing, since one of the expected advantages of living vaccines, chiefly because of the experience with yellow-fever vaccination, was that they would give a more durable immunity. However, as the authors observe, neutralizing antibody titres may not measure immunity, especially as they take no account of possible local immunity in the intestine.

The third paper on live virus vaccines in this issue (p. 1184) is a balanced review of the present position by Professor Dick and Dr. Dane. Thousands of people have been vaccinated with live attenuated virus, and experience shows that there is little likelihood that the vaccinated subject will himself suffer any ill effect: none so far are known to have done so. The possible danger is to contacts, who may become infected from the vaccinated. That contact infection with the live vaccine strains occurs has been repeatedly shown. If such strains remain attenuated, contact infection, by disseminating them among the population, might supplant wild virulent strains and raise the general immunity; but if on passage the vaccine strains regain appreciable virulence, then they might lead to paralytic cases of poliomyelitis among those to whom they spread.

Although their discussion does not take account of the Sheffield experience, Dick and Dane emphasize the importance of defining the limits of safety of living attenuated vaccines as the immediate aim of further trials. Much remains to be done before any firm assumption on the safety of widespread use of live virus vaccine is justified. Under the more or

[1] W.H.O. Technical Report No. 145, 1958.
[2] Courtois, G., Flack, A., Jervis, G. A., and Koprowski, H., *Brit. med. J.*, 1958, **2**, 187.
[3] Dane, D. S., Dick, G. W. A., Connolly, J. H., Fischer, O. D., and McKeown, Florence, ibid., 1957, **1**, 59.
[4] Sanders, F. K., Huppert, J., and Hoskins, J. M., *Symposia Soc. exp. Biol.*, 1958, No. XII, p. 123.

less controlled and special circumstances of laboratory study, the level of neurotropic virulence can be varied in either direction, or held approximately steady. It is not known whether attenuation is a process of mutant selection, as the plaque-picking technique assumes, or whether it is a phenotypic change induced by environment, of the kind seen with encephalomyocarditis, another R.N.A. virus.[4] Nothing is known of the nature of the annual change in poliomyelitis which, in temperate countries, brings on the polio season in summer and autumn. It is possible that in nature strains of virus change their virulence in either direction as freely as they do in the laboratory. Dick and Dane record an interesting and highly pertinent observation on the high virulence to monkeys of virus isolated from paralytic cases compared with the much lower monkey virulence of virus presumably of the same strains isolated from contacts of these cases.

Many different pieces of circumstantial evidence seem to indicate that the power of the polio virus to paralyse is a most unstable characteristic, that fluctuations in this power occur in nature for reasons which are entirely unknown, and therefore are unpredictable. The "theoretical expectations of safety" can, in the opinion of some authorities, hardly be said to be firm enough to justify any trials on human beings other than those made on small numbers of volunteers in circumstances such that the spread of the virus can be closely watched and effectively controlled. Such trials are wholly practicable, and are needed to shed further light on this difficult and complex problem. At this stage "trials on hundreds of thousands of people" may or may not be carried through without ill effect. It is difficult to see how they can tell us much about the protective power of the vaccines; and to attempt to apply the results observed in tropical countries with an initially high incidence of poliomyelitis virus to temperate or other countries where the disease behaves differently might, for all we yet know, prove disastrous. The whole history of poliomyelitis vaccination has a tendency to run at a pace decided by politics and the press: in this respect it is very different from the history of diphtheria immunization, which did not become general until the scientific basis of it had been fully worked out. The best chance of achieving a sound assessment of live poliomyelitis vaccines lies in a continuation of careful small-scale studies like those discussed in the three articles in this issue and the many which have been made in the United States by the American workers who have pioneered in this field.

WILD GAME AND SLEEPING SICKNESS

In the Croonian lectures of 1915 Sir David Bruce[1] described the isolation of polymorphic trypanosomes from 14 wild animals out of 180 examined in Nyasaland. He was of the opinion that the organism was identical with the one responsible for Rhodesian sleeping sickness, and that wild game animals must constitute a dangerous reservoir of the infection. Further isolations were made by British and German workers, but all these observations, including Bruce's, were based on the assumption that a single species of trypanosome was concerned; we now know, on the contrary, that two species exist, identical in appearance, one of which is infective to man and animals (*Trypanosoma rhodesiense*) while the other is infective to animals alone (*T. brucei*). The only way of distinguishing the two species is by inoculating them into man, in whom *T. rhodesiense* alone will take. This essential test was not applied by the early workers, and their isolations may have been of either species. The same doubt shadows the experiments of H. L. Duke[2] in Uganda, where he reported the presence of *T. gambiense* in the sitatunga (swamp bushbuck). Nevertheless, epidemiological evidence was accumulating that game was indeed a reservoir of the human parasite: repeated examples occurred of hunters going into game country totally uninhabited by man and returning not only with the trophies of the chase but with Rhodesian sleeping sickness. Shortly before his death, C. H. N. Jackson[3] summarized his experience in Shinyanga and came to the conclusion that wild animals must form a reservoir of the disease in nature, basing this both on the history of cases and on the isolation of true *T. rhodesiense* from tsetse flies caught in the bush.[4] The susceptibility of antelopes to *T. rhodesiense* was proved beyond question by J. F. Corson, H. Fairbairn, and K. C. Willett, working at the Tinde laboratory of the East African and Trypanosomiasis Research and Reclamation Organization, and the strain was maintained in these animals by blood or fly passage continuously for ten years, at the end of which time it proved to be still infective to man.[5]

Many people were satisfied with this circumstantial evidence, but final proof was still lacking, and two attempts have recently been made to fill the lacuna. M. T. Ashcroft[6] in Tanganyika inoculated the blood of 47 wild animals into rats and recovered a polymorphic trypanosome from a single hartebeeste; this proved to be non-infective to man. In this issue of the *Journal* (p. 1203) R. B. Heisch, J. P. McMahon, and P. E. C. Manson-Bahr report the actual presence of *T. rhodesiense* in wild game. Using thirty times the quantity of blood that Ashcroft employed and with the resources of the experienced Division of Insect-borne Diseases of the Kenya Medical Department at their disposal, they obtained from a bushbuck a polymorphic trypanosome which was later inoculated into (and infected) a member

[1] Bruce, D., *Lancet*, 1915, **2**, 1.
[2] Duke, H. L., *Sleeping Sickness Bull.*, 1912, **4**, 171.
[3] Jackson, C. H. N., *Trans. roy. Soc. trop. Med. Hyg.*, 1955, **49**, 582.
[4] MacKichan, I. W., ibid., 1944, **38**, 49.
[5] Willett, K. C., and Fairbairn, H., *Ann. trop. Med. Parasit.*, 1955, **49**, 278.
[6] Ashcroft, M. T., *Trans. roy. Soc. trop. Med. Hyg.*, 1958, **52**, 276.
[7] Potts, W. H., *Times Science Review*, 1958, no. 28, 13.

of their staff who had remained behind in Nairobi, far from any endemic zone of the disease. The main story of sleeping sickness in Africa is thus brought to a conclusion, though many details still await clarification. It is a paradox that this successful experiment was performed in a region where *T. rhodesiense* was absent until 1940, when it overflowed into Kenya, in the human form, from the epidemic raging in Uganda; wild animals must have become infected later, and once more we have an example of a zoonosis *hors de ligne*.

Confirmation that wild animals are a reservoir of sleeping sickness should not provide to-day ammunition for the bloodthirsty exponents of game destruction for the control of the disease. The facilities offered by the synthetic insecticides, the subtle introduction of sterile male tsetse flies,[7] or prophylaxis with the new drugs, render this crude approach as unnecessary as the removal of a population. The beautiful African fauna should remain undisturbed.

CARDIOLOGY IN THE N.H.S.

A year or so before the N.H.S. came into being in 1948 a committee on cardiology of the Royal College of Physicians of London reported on the training of cardiologists and on the practice of cardiology in hospitals and in the Health Service that was to come. This month the College has issued a report of another committee on cardiology appointed in 1957 "to review and consider the implementation of the report of the Committee on Cardiology of April, 1947." Of the eighteen members of the later committee nine served on the earlier one. That there is some dissatisfaction about the place of cardiology in the N.H.S. might be assumed from the present report. Many well-trained young cardiologists, it states, are not in a position to use their skill, and this is already deterring the best young men from seeking appointments in cardiac departments. This leads to the suggestion that "the Ministry of Health could with advantage give the same official recognition to cardiology as it does to neurology and certain other specialties." Because a large proportion of the work of physicians in the N.H.S. is concerned with circulatory disablement in some form, the committee regards the investigation and treatment of cardiovascular disorders a necessary part of the work of general physicians, who should, however, always be able to call upon a fully equipped specialist department to help in difficult and complicated cases.

The report gives the committee's recommendations on the training of cardiologists and on the establishment and staffing of cardiac departments. Five years is suggested as the minimum period of training after the conclusion of the trainee's junior hospital appointments: two years of this period should be spent as a registrar or junior teacher in a department of general medicine, two years should be spent in a cardiac department, and one year in research. There should be a department of cardiology at one of the main teaching hospitals of each medical school, and outside the teaching hospitals a cardiologist should be appointed to every major hospital centre and to every hospital where surgery of the heart is performed. As to the smaller hospital centres, the report urges that a first-class opinion should be available for every patient with a heart disorder needing expert advice: "this means that in every area where access to a major hospital centre is not easy, one or more cardiologists should be appointed among the physicians working in this area." The report is not without glimpses of the obvious: for instance, it outlines the ways in which the department of cardiology should establish liaison with departments of cardiac surgery, child health, and obstetrics, and in its recommendations on accommodation it states that "there should also be adequate room for patients waiting." But, in general, the report gives the Ministry clear guidance on how to provide the best possible cardiological service within the N.H.S.

SPEEDING THE TAN

A tanned skin has come to be regarded as a sign of vigorous health and, lately, as a social asset, for it commonly betokens a visit abroad to those parts of Southern Europe where the sun is less sparing with his favours than in Britain. The cosmetic manufacturers have therefore provided numerous preparations designed to permit tanning while reducing the risk of sunburn, and others which attempt with suitable pigments to simulate a natural tan. Now a drug which increases and accelerates tanning may soon be introduced[1] in the United States.

The drug, methoxypsoralen, has an interesting history. Extracts of the plant *Ammi majus*, containing this substance, were employed in Egypt as an ancient folk remedy for vitiligo. Reports of the first scientific investigation of the photosensitizing properties of extracts of *Ammi majus* appeared in 1947[2] and the active ingredients were isolated and identified. The first clinical trials were soon carried out, and encouraging results were claimed in the treatment of vitiligo. The psoralens have since been prescribed in dermatological clinics in many countries. There is no doubt that these substances applied topically or taken by mouth before the skin is exposed to ultra-violet light will induce formation of pigment in some areas of vitiligo. However, the response in the individual case is unpredictable; treatment has to be prolonged and is extremely time-consuming; and even if re-pigmentation is achieved it may not be permanent. It has been estimated that only one in seven patients treated obtains satisfactory re-pigmentation. A. Jarrett and G. Szabo[3] showed that a pigmentary response is obtainable only in those areas in which some melanocytes remain, and this may explain the many failures. The incidence of unpleasantly severe inflammatory reactions to the topical application of the

[1] *J. Amer. med. Ass.*, 1958, **167**, 2081.
[2] Fahmy, I. R., and Abu-Shady, H., *Quart. J. Pharm.*, 1947, **20**, 281.
[3] Jarrett, A., and Szabo, G., *Brit. J. Derm.*, 1956, **68**, 313.
[4] Sulzberger, M. B., and Lerner, A. B., *J. Amer. med. Ass.*, 1958, **167**, 2077.

psoralens is so high that this treatment has been generally abandoned. Oral administration produces less spectacular side-effects, but nausea, diarrhoea, headache, and depression are not uncommon. Though no better treatment for vitiligo is available, most dermatologists would now agree that the psoralens should be reserved for selected cases treated under close supervision and that these drugs are mainly of value in research.

While the psoralens will induce a much more consistent pigmentary response in normal skin than in vitiligo, it is neither completely constant nor predictable, and the risk of side-effects is equally great. M. B. Sulzberger and A. B. Lerner[4] point out that we do not know whether prolonged or repeated ingestion of psoralens exposes the subject to other hazards. We do not know, for example, what effect, if any, these drugs may have on the development of chronic solar degenerative changes, including carcinoma. After critical review of the available evidence it is impossible at present to justify the use of the psoralens merely to acquire an impressive South of France tan in an average English summer.

DETECTION OF OVULATION

Since the human ovum does not survive after ovulation for more than a few hours—less than twelve, it is generally believed—conception is unlikely to occur unless coitus takes place within a short time of it. Couples seeking advice on infertility are always told to have sexual relations during the fertile phase of the menstrual cycle, but to define that phase, except in rather general terms, has proved none too easy. The most commonly used adjunct has been the basal temperature record, which characteristically shows a mid-cycle rise and post-ovular plateau caused by the progesterone secreted by the corpus luteum. The temperature rise, "thermal shift," to use the current transatlantic expression, is usually described as being immediately preceded by a temperature drop—the "ovulatory dip"—but this is exceptional and probably fortuitous, though often said to indicate the precise day of ovulation. The inconstancy, if not irrelevance, of the ovulatory dip, and the fact that the thermal shift occurs *after* ovulation (as has been shown most elegantly by the hormone-excretion studies of J. B. Brown and colleagues[1]), make the basal temperature record no more useful for detecting the day of ovulation—except in retrospect—than would measurement of the daily output of urinary pregnanediol, which also reflects progesterone secretion. Detection of the urinary oestrogen peak at ovulation would be more precise but is obviously not a practical proposition. Nor, scarcely, is the daily collection and examination of vaginal smears, though by this means it may be possible to pin-point the day of ovulation. The rat-ovary hyperaemia test of Farris,[2] which, in the hands of its author, has facilitated precise prediction of the day of ovulation, is also far too cumbersome for general practical use; moreover, some other workers have not had the same success with it.

In view of the shortcomings of these methods of detecting ovulation, much interest attaches to the observation of C. H. Birnberg, R. Kurzrok, and A. Laufer[3] that by inserting into the vagina daily a strip bearing glucose oxidase, which detects the presence of glucose ("tes-tape," the British counterpart of which is "clinistix"), the day of ovulation can be detected by a sharp rise in the concentration of glucose in the cervical secretions. J. B. Doyle[4] has modified this procedure so that the woman can carry it out herself and so select the day of ovulation without any medical intervention. That this change in glucose concentration really indicates the occurrence of ovulation would seem to be attested by Doyle's finding freshly ruptured follicles in two women subjected to laparotomy (for entirely independent reasons) on the day of maximum "tes-tape" colour, and by the prompt occurrence of conception in 23 out of 27 women subjected to A.I.D. by Birnberg and colleagues on days chosen in the same way. For control of fertility by the "rhythm" method, detection of ovulation by this technique would seem to offer an important advance in safety and precision to the patient who chooses to use it.

[1] Brown, J. B., Klopper, A. I., and Loraine, J. A., *Proc. roy. Soc. Med.*, 1958, **51**, 556.
[2] Farris, E. J., *Human Ovulation and Fertility*, London, 1956.
[3] Birnberg, C. H., Kurzrok, R., and Laufer, A., *J. Amer. med. Ass.*, 1958, **166**, 1174.
[4] Doyle, J. B., ibid., 1958, **167**, 1464.

TRAVELLING SCHOLARSHIP FOR GENERAL PRACTITIONERS

In the Association Notices this week (*Supplement*, p. 212) particulars are given of a scholarship for which competition among general practitioners is likely to be keen. The trustees of the Claire Wand Fund are offering a travelling scholarship of a maximum value of £600 to a general practitioner prepared to spend 6–8 weeks in the U.S.A. and Canada and to attend the Second World Conference on Medical Education in Chicago early next September.[1] The Claire Wand Fund was established in memory of the wife of Dr. S. Wand, the present Chairman of Council, and the capital sum from which the Fund's income is derived was contributed mainly by general practitioners in recognition of the outstanding services rendered to the medical profession by Dr. Wand and Dr. D. P. Stevenson during the negotiations leading to the Danckwerts award. The income of the fund is applied "for the purpose of further education of medical practitioners who are predominantly engaged in general practice," and the award of the travelling scholarship now announced is to enable a general practitioner to study what is done for the further education of general practitioners in Canada and the U.S.A. In submitting their applications general practitioners should describe what studies they propose to undertake in North America: applications should be submitted to the secretary of the Fund at B.M.A. House not later than January 31, 1959.

[1] See *British Medical Journal, Supplement*, 1958, **1**, 194.

Drug Treatment of Disease

DRUG TREATMENT OF PARKINSONISM

BY

MACDONALD CRITCHLEY, M.D., F.R.C.P.

Neurologist, King's College Hospital

The drug treatment of Parkinsonism is merely palliative and not curative. Nevertheless, by steadily continued medication wisely prescribed and controlled, some of the more distressing symptoms may certainly be alleviated. As might be expected, cessation of drug treatment is followed by a relapse or exacerbation. Some of the symptoms of Parkinsonism prove to be more obstinate than others: for example, tremor is particularly difficult to check; whereas rigidity, and feelings of weakness or heaviness of the limbs, usually respond moderately well to medication.

The recent introduction of surgical methods of alleviation will probably not influence the scope of drug treatment in this malady. Parkinsonism, be it remembered, is a progressive affection, and surgery is scarcely likely to stem its advance. Even a fairly successful surgical intervention does not render the patient altogether free of symptoms; drugs will still be needed, even though the dosage may be smaller.

As in the case of many other chronic disorders, patients vary in their reaction to the disease. They differ in their standards of personal discomfort. They also differ in the rate of advance of the disease, and in respect of the individual sensitivity towards a particular drug. A preparation which suits one patient—or even the majority—may upset another. Some patients seem to be intolerant of almost every medicament that the practitioner can devise; fortunately, however, such troublesome cases are comparatively uncommon.

Since the end of the second world war the type of drug therapy used in cases of Parkinson's disease has notably changed. Up to about 1947 reliance was placed chiefly upon preparations of the Solanaceae—hyoscine, hyoscyamine, atropine, belladonna, stramonium. Since that date these drugs have been virtually superseded by a number of synthetic preparations. These are claimed to be more effective—as indeed they generally are—and also to be complicated by fewer unpleasant side-effects. These comparatively new preparations fall into two main classes—namely, antispasmodics and antihistaminics. Some practitioners prefer to give these two classes of drug together.

Antispasmodics

Physicians with a wide experience of the drug treatment of Parkinsonism not unnaturally differ somewhat in their choice of these remedies. It would probably not be an exaggeration, however, to state that one preparation stands out as the drug of choice in the experience of most practitioners. This is *benzhexol* ("artane," "pipanol"), usually known in America as trihexyphenidyl. It is benzhexol which appears to suit best the greatest number of patients with Parkinsonism. As with almost every form of medication, the patient should start with small doses and then gradually increase them as his tolerance increases. Benzhexol is marketed in tablets of two strengths—namely, 2 mg. and 5 mg. Ordinarily the best policy is to start with one tablet of 2 mg. twice daily. The dosage may be increased at the end of a week to thrice daily. Thereafter it can slowly be augmented. Some doctors prefer to rely exclusively upon the 2-mg. tablets rather than the 5-mg., and to prescribe if need be two or three such tablets, twice, thrice, or even four times a day. Quite high dosage is at times possible, though rarely so.

Side-effects of benzhexol sometimes appear in sensitive subjects even with small doses, but fortunately not often. With larger doses, nausea may occur and even vomiting. Even more common is a complaint of vague cephalic sensations, sometimes described as muzziness, heavy-headedness, or a tightness within the head. This particular symptom is often relieved by tablets of amphetamine combined with acetylsalicylic acid.

After benzhexol the second place among the most favoured drugs is less easy to identify. Perhaps the next most useful drug—though not as well known as benzhexol—is *benztropine methanesulphonate* ("cogentin"). This is a comparative newcomer, but it is already proving useful. Perhaps it influences tremor better than any other available preparations. This drug is dispensed in tablets of 2 mg. One may start treatment with half a tablet (i.e., 1 mg.) once a day, and thereafter cautiously the dosage may be increased. The drug acts slowly, and, being long-acting and cumulative, a single morning dose may prove adequate. Side-effects include some dryness of the mouth, nausea, and occasionally skin rashes.

Another deservedly popular drug, almost as valuable as benzhexol, is *procyclidine* ("kemadrin"). The clinical action is very similar to that of benzhexol. It is put up in 5-mg. tablets and treatment may be started with half a tablet twice a day until such time as one is sure that the drug is proving serviceable. Among the rare side-effects are dryness of the mouth, blurred vision from pupillary dilatation, and dizziness.

Some neurologists, however, are inclined to look upon *ethopropazine* ("lysivane") as the most useful drug. Some patients with Parkinsonism prefer this to benzhexol, just as some others (larger probably in number) would vote contrariwise. Ethopropazine is chemically related to an older preparation—namely, diethazine—but it is more active and yet less toxic.

After the foregoing drugs there is a considerable gap in the utility of the other pharmacological agents. Here one can include caramiphen or phenylcyclopentane carboxylic acid ("parpanit")—actually the first of the "newer" drugs which appeared after the war. A preparation which seems to be gaining favour is β-dimethylaminoethyl-2-methylbenzhydryl ether hydrochloride ("disipal"). This drug is dispensed in tablets of 50 mg., and the ordinary dose is four such tablets a day, cautiously increased to eight. It is said to act somewhat as a euphoriant, and to possess only the usual side-effects, which are readily overcome. The combination of this drug with ethopropazine has recently been advocated as an efficient remedy.

Antihistaminics

In addition to the foregoing spasmolytic drugs, there are various antihistaminics which are often given in cases of Parkinson's disease. Though at times administered alone, more often they are prescribed in association with one of the spasmolytics—e.g., benzhexol—and the combination is indeed often a useful one. Most popular of this class of drugs in the treatment of Parkinsonism is diphenhydramine ("benadryl"), put up in capsules containing 50 mg. The ordinary dose is one capsule one or four times daily. The commonest side-effect is drowsiness, and indeed this fact

MA5682

'Stemetil'

trade mark *brand*

PROCHLORPERAZINE MALEATE

for the management of migraine

'Stemetil' is indicated for the prevention of true migraine and to lessen the frequency or severity of attacks. 'Stemetil' is also indicated in Ménière's syndrome, other labyrinthine disorders and for nausea and vomiting.

Detailed information is available on request.

PRESENTATIONS

Tablets of 5 mg. and suppositories of 25 mg.

1·25% Solution for injection.

MANUFACTURED BY M&B **MAY & BAKER LTD**

An **M&B** *brand Medical Product*

DISTRIBUTORS: PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD · DAGENHAM

Lederkyn*

SULPHAMETHOXYPYRIDAZINE

*REGD. TRADEMARK

a real step forward with 'once-a-day' sulpha therapy

Full chemotherapeutic potential—antibacterial spectrum equivalent to that of sulphadiazine.

High, sustained blood levels, ensuring continuous, not intermittent, antibacterial action.

Low 'once-a-day' dosage suffices to maintain the average adult or child patient.

Lederkyn Acetyl pediatric suspension
250 mg./5cc. Bottles of 2 and 16 fl. oz.

Lederkyn tablets 0.5 gm. Bottles of 24, 100 and 500

Lederle

LEDERLE LABORATORIES DIVISION
Cyanamid OF GREAT BRITAIN LTD., London, W.C.2

CYANAMID

may be utilized with advantage; the patient with Parkinsonism who has difficulty in getting off to sleep may well take 50–150 mg. (i.e., 1–3 capsules) on retiring. Another popular preparation is phenindamine ("thephorin") given in doses of 100 to 200 mg. either alone or preferably combined with benzhexol (8–10 mg. daily) or procyclidine (5–15 mg. daily). Thenindamine is marketed in 25-mg. tablets.

Psychiatric Symptoms

Although the phenomenon is quite rare, some patients unfortunately develop flamboyant psychiatric symptoms when taking these post-war remedies. In such cases it seems as though switching from one preparation to another does not meet the situation, and these types of drug simply have to be withheld altogether.

These unusual symptoms comprise in the first place a gradually mounting degree of confusion—of which the patient, incidentally, is fully aware. Then develop ideas of reference, at first regarded by the patient as foolish, but gradually increasing in plausibility. Next come vivid fantasies both in the sleeping and the waking states. Lastly an actual hallucinosis supervenes, with visions of imaginary animals and people, usually of a bizarre and even horrific nature. Tactile and auditory hallucinations are less common. Nothing short of complete abstinence from drug therapy is effective, and the patient regains intellectual normality only at the cost of enhanced physical disability.

Solanaceous Drugs

Finally, it is worth bearing in mind the older, that is pre-war, remedies which used to help patients with Parkinsonism. They still deserve a place within our armamentarium not only for those cases in which the newer drugs are badly tolerated, but also as an adjuvant. In other words, combinations of the antispasmodics with the solanaceous drugs may prove to be quite useful. Of the latter drugs, hyoscine hydrobromide was the one most often used. It was generally prescribed in initial doses of 1/150 gr. (0.4 mg.) thrice daily, often in a mixture to which potassium bromide 5–10 gr. (0.3–0.65 g.) and tincture of nux vomica 10 minims (0.6 ml.) were added. Sometimes it was prescribed in the form of a tabella which was allowed to dissolve under the tongue.

Atropine or belladonna were also given. Patients with the post-encephalitic types of Parkinsonism seemed to respond better than cases of paralysis agitans—but that, of course, is the common experience and applies to all forms of drug therapy. Those patients who are particularly incommoded by excessive salivation are often helped most by atropine or belladonna. Large doses are needed, and it is difficult to avoid such complicating symptoms as blurred vision, palpitations, and nausea. When employing belladonna it is worth remembering that, while young patients tolerate this drug well, some are naturally sensitive to it. In these cases the side-effects may be so distressing as to preclude the drug, and the major complications include psychiatric states of confusion and mild delirium.

Formerly some attention was paid to what was called the Kleeman treatment. At times it was beneficial and it may still have a small place in the modern therapy of Parkinsonism. The object here was to give the patient rapidly increasing amounts of atropine so as to condition the patient to comparatively high doses. Kleeman would begin with 0.5 mg. of atropine daily in the form of a ¼% solution of atropine sulphate given in two doses (one drop containing 0.25 mg.). This is increased by 0.5 mg. daily, spread over three doses, so long as any clinical improvement is produced. Thereafter the dose is gradually reduced in order to determine the optimal amount. Kleeman found this to be as a rule 3 to 7 mg. of atropine daily (though some other physicians used even higher doses).

There were several useful and "elegant" preparations on the market which were often of great service in the treatment of Parkinsonism. They were relatively mild in effect and, being largely devoid of complications, could be prescribed with considerable latitude. Some of these preparations combined in pillule or tablet form small amounts of hyoscine, atropine, and hyoscyamine.

Lastly, stramonium was a most useful palliative treatment, especially in the post-encephalitic varieties of the disease. By shrewd prescribing, it was possible gradually to increase the dosage and to attain comparatively high and clinically effectual amounts. Though the tincture of stramonium was often prescribed—doses starting at 10 minims (0.6 ml.)—experience showed that the dried extract of the drug (ext. stramonii sicc., *U.S.P.*) was the most effective. Here the initial dosage was ordinarily 0.25 g. three times a day. The side-effects of stramonium resemble those of atropine, but they were less common and milder.

A. F. Hurst, who never shrank from prescribing drugs in high dosages, used to advocate the giving of large amounts of stramonium, by dint of gradual augmentation coupled with the administration of pilocarpine. Treatment would begin by the patient taking 10 minims (0.6 ml.) of tinct. stramonii in ½ fl. oz. (14 ml.) of water on waking, after lunch, and after tea. If stiffness interfered with sleep, a fourth dose was given to the patient as he retired. On alternate days 1 drachm (3.5 ml.) would be added to each dose, so that in eight days the dose would be doubled. This gradual increase would go on until the patient complained of blurred vision or undue dryness of the mouth. Pilocarpine nitrate, 1/10 gr. (6.5 mg.), would then be added to the latest dose of stramonium, and once more the increase of 1 drachm (3.5 ml.) on alternate days would go on, until slight toxic symptoms developed.

EARLY DISTURBANCE OF BEHAVIOUR IN RELATION TO MENTAL DEFECT*

BY

BRIAN H. KIRMAN, M.D., D.P.M.

The Fountain Hospital, London

In the majority of cases of mental defect there are no specific or qualitatively distinct forms of behaviour which could be the basis for early recognition of abnormality. In most instances there exist merely quantitative changes; the behaviour of the child has not reached the level of development which might be expected in view of the chronological age.

Value of Early Assessment

I would like first to ask what is the purpose of the medical adviser in attempting to make an early diagnosis of mental defect and, indeed, to question whether such attempts are always wholly praiseworthy. For practical purposes it is possible to distinguish between two levels of mental defect, high grade and low grade. The former term covers the feeble-minded; the legal validity of this term as at present used has been called into question, and there is some danger that it may be replaced by the even more elastic word "psychopath." The low-grade patients include the idiots and imbeciles, and for those who prefer some attempt at numerical estimation an intelligence quotient of 50 is usually taken as marking the borderline between the high- and low-grade groups.

In regard to adult mental defectives, more than half the population of institutions is made up of high-grade cases (O'Conner and Tizard, 1956). In the case of children, however, the position is quite different, since the Education Act of 1944 removed the necessity to

*Based on lecture to Assistant County Medical Officers, Essex, 1957.

certify as mentally defective children in need of special education. In considering the question of mental defect in young children, therefore, we are concerned only with low-grade cases—that is, with idiocy and imbecility. The school medical officer may, however, also be concerned with the question of educational retardation and the need for special education.

I understand that the position in the area with which I am here concerned is that special schools are not available for the educationally subnormal (E.S.N.) until they reach the age of 7 years. An adjacent local authority, on the other hand, has taken the step of providing a nursery school for the E.S.N. Let me say at once that there is a question of expediency here. From a practical point of view, and faced with pressure of social circumstances, it may be easier to help a supposedly backward child in areas where special facilities are provided from an early age. So far as principle is concerned, however, a decision regarding special schooling at the age of 7 years seems much more desirable. By that age it will have been found by experience what the child's capabilities in the way of learning really are, and some form of assessment of his probable future progress will be possible. It seems very undesirable that a child should be classed at the age of 2 or 3 years as E.S.N. or even occasionally as feeble-minded, since an analysis of the total situation in such cases will more often reveal a disturbed background than a disturbed child (Hilliard and Kirman, 1957). Adverse social factors play a major part in causing such cases to be considered retarded (Craib and Woodward, 1958 ; Kirman, 1958). It is particularly important to remember that once such a decision has been made the label tends to stick to the child throughout his subsequent career regardless of all provision for reassessment.

Anatomical Basis for Mental Defect

Tests are of value only if they predict subsequent attainment, and the predictive value of tests of ability under the age of 5 is limited (Vernon, 1955). If, therefore, we are attempting to assess in the case of a particular young child whether or not he is mentally defective on the basis of unusual behaviour it seems desirable to confine our attention to gross defect. It has long been considered that in most cases of gross mental defect there is a corresponding gross abnormality of the brain. Berry (1938) noted the marked reduction in weight and size. Recent work (Crome, 1954) on a big series of unselected cases has confirmed that obvious lesions are usually present. Figs. 1 to 5 illustrate some of the abnormalities observed. This being so, it will be found that in a considerable number of cases a detailed history and a careful physical examination will provide evidence of abnormality to supplement the story of abnormal behaviour. This applies equally to cases due primarily to genetic factors (primary amentia) and to those ascribed to environmental influences (secondary amentia). In a proportion of cases, however, the cerebral abnormality is discovered only after death, and during life there were no neurological symptoms and no history of illness or untoward event which might have produced the abnormality. In these cases the only symptoms of the cerebral defect are those which are summed up as "mental defect."

First Symptoms Noted By Parents

The data shown in the accompanying Table are derived from the social histories of 233 patients admitted to hospital, usually under the age of 5 years, as mental defectives. In each case the leading symptom complained of by the parents is taken. In some instances there was no specific complaint, merely a general statement that the child was slow in developing, but in the majority more specific information was available. The symptoms leading to the first recognition of the mental defect have been shown at the time at which they came to the notice of the parent. In

FIG. 1.—Hydrancephaly. Very little functioning brain cortex. Complaint of constant screaming and taking no notice at 3 months.

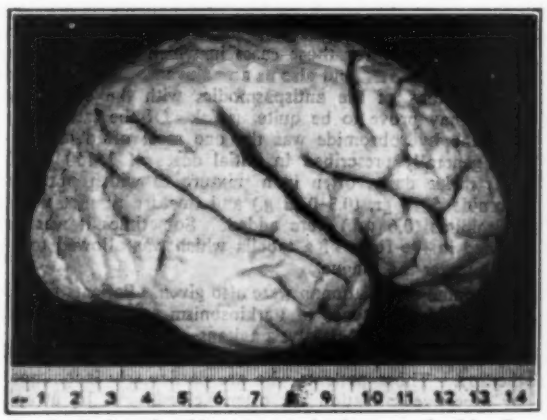


FIG. 2.—Pachygyria with very poor development of sulci. Convulsions at 3 months followed by regression.

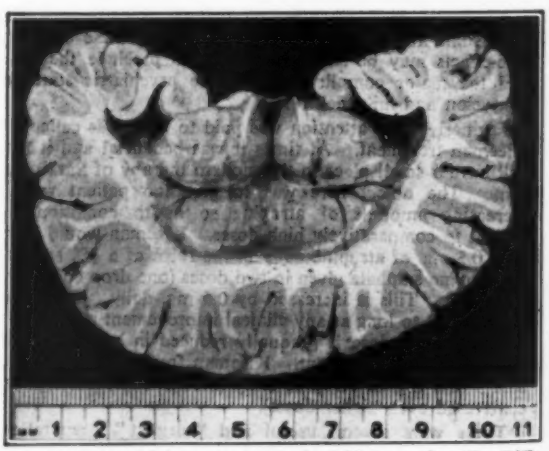


FIG. 3.—Frontal lobes not separated. Did not suck well. Difficult to feed from birth.

many cases this was when the parents first felt sure about the defect: they had often had a vague suspicion previously that all was not well. This was particularly so, for example, in the case of twins where the normal child was available for comparison. In many histories additional details have been supplied, but it was thought that a clearer picture would emerge if only the first symptoms which arrested the attention of the parent were recorded.

Table Showing Time of Appearance of First Symptoms of Mental Defect in 233 Children

Symptom	Age in Months							Total
	Birth	Under 3	3–5	6–11	12–23	24–35	36–48	
Physical features	25	18	8	5	4	1	—	61
Eye defect	4	5	9	5	4	2	—	29
Feeding difficulties	3	1	—	—	—	—	—	4
Quiet	—	2	—	—	1	—	—	3
Cerebral palsy	—	1	5	—	—	—	—	6
Slow	—	1	14	16	9	3	—	43
Not taking notice	—	1	6	1	—	—	—	8
Not sitting	—	—	14	15	5	—	—	34
Screaming	—	1	4	1	2	—	—	8
Peculiar movements	—	—	4	—	—	—	—	4
Not crawling	—	—	2	—	—	—	—	2
Not walking	—	—	—	1	10	5	—	16
Restless	—	—	—	1	3	1	—	5
Not using hands	—	—	—	1	—	—	—	1
Head banging	—	—	—	—	1	—	—	1
Not speaking	—	—	—	—	1	4	—	5
Not playing with toys	—	—	—	—	1	—	—	1
Destructive	—	—	—	—	—	1	—	1
Not clean	—	—	—	—	—	—	1	1

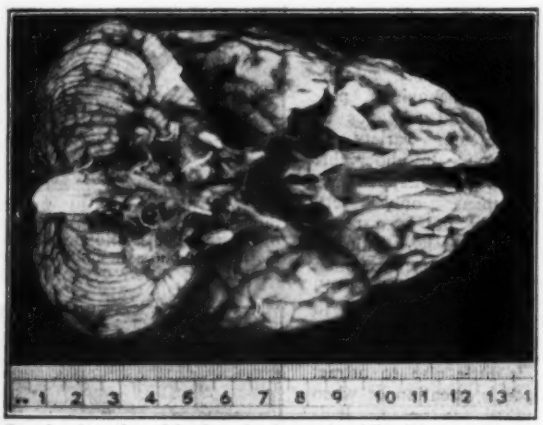


FIG. 4.—Atrophy of brain. At 6 months child did not seem to see or hear.

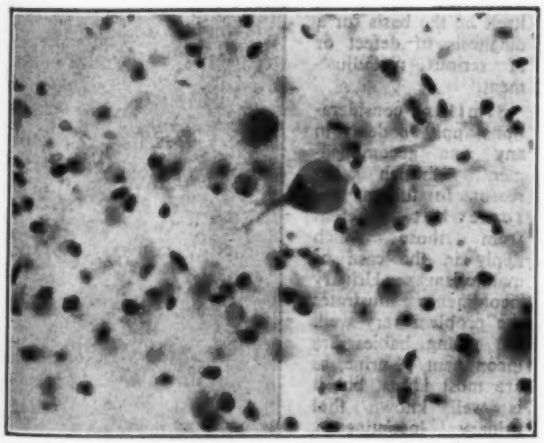


FIG. 5.—Same case as 4, showing lipoidosis. A case of cerebro-macular degeneration.

The biggest single group of cases was recognized by the parents or by their medical advisors on the basis of physical abnormalities, and this was also the group most readily recognized at birth, as might be expected, since the range of behaviour of the newborn baby is so limited. The commonest of the physical abnormalities recognized in this way was mongolism, but the group also includes such conditions as microcephaly and hydrocephalus. Another big group of cases was noticed early on account of "eye defect." Some of these children were blind, but more often they seemed blind to the parents at this early stage. Their eyes did not follow a light or they failed to fix objects with their eyes, or, slightly later, failed to turn their heads towards objects displayed. The groups which first came to attention because of feeding difficulties, quietness, or cerebral palsy were smaller, and the next big group is that merely classed as generally slow. This is obviously a residual collection due either to failure of the parent to particularize or simply to realization of the fact that this was indeed the most accurate description of the position, that the child was slow in all his accomplishments.

In the "not taking notice" group the emphasis is on the lack of emotional response, whilst the big "not sitting" group begin to worry the parents because of failure to reach this important and well-recognized "milestone" at the appropriate time. A smaller group of parents had suspended judgment until the child failed to walk at the normal time, and only five had delayed still further until the child had reached the appropriate time for beginning to talk. Five patients were noticeable because of restlessness and single cases because of other symptoms.

In glancing through the list of symptoms perhaps the most striking thing is that most of them are negative—that is, simply a statement that a child failed to do a certain thing at a certain time. Only 18 cases drew attention to themselves because they did something which was unusual. Perhaps a more correct statement would be that they persisted in doing something after the time for this form of activity had gone by; this applies, for example, to the fine repetitive movements of the fingers which are normal in a young baby but which are later described in imbeciles and idiots as "digital mannerisms." These patients with positive symptoms included the "screaming" group, those with "peculiar movements," restlessness, head banging, and destructiveness. The majority, then, exhibit simply a quantitative defect or retardation of behaviour development which may be given a quantitative expression on the basis of any of the recognized scales of norms.

Psychosis or Mental Defect?

Difficulties may arise in the interpretation of the abnormal behaviour noted in both the majority and the minority groups. For example, it is well known that on occasion a child who fails to sit, stand, or talk at the usual time may yet prove to be above average in intelligence. It is, however, the minority group whose leading abnormality consists of qualitatively abnormal behaviour who are most difficult to understand. On the one hand the symptoms may simply be evidence of retardation. This may be true of restlessness. Normal children are restless, but they are usually capable of being trained to some extent, so that the expression of the restless tendency can sometimes be limited by parental influence. This implies, however, capacity to respond to "atmosphere," to adult approval or disapproval, and to other factors in the social environment. Very backward children are slow in acquiring this capacity, and the abnormality is not so much that they are restless as that they are inappropriately and persistently restless in an unmodifiable manner.

On the other hand such symptoms as restlessness or "peculiar movements" are also characteristic of children with psychotic and neurotic illnesses. It is often a matter of extreme difficulty to distinguish between simple mental defect and psychosis in a young child. To some extent the distinction is one of definition. In any considerable group

of mentally defective children there is a small minority who might more aptly be described as psychotic. They function socially at idiot level and fail to co-operate in standard tests to such an extent as to secure a very low rating. On the other hand, careful observation may lead to an impression that the child has considerable capacities which are unused or are utilized in a negative manner. For example, a child who attracts attention by head banging may display other forms of negativistic behaviour. This behaviour may be nicely timed in such a manner as to indicate considerable discernment of social situations. The appearance of a stranger or any other slight derangement of the usual order of events may be followed by refusal of food or by a display of head banging. Obsessional tendencies in such patients may likewise indicate extreme nicety of perception.

The position is still further complicated by the fact that it is not rare for a backward child to develop superimposed psychotic features. Similarly, withdrawal and "autism" may be seen in children who are known to suffer from epilepsy or to have good evidence of structural abnormality of the brain.

It should also be pointed out that in psychotic children simple failure to carry out normal activities may also be a conspicuous part of the picture. The commonest form of infantile psychosis is of the schizophrenic type with poverty of social contact, and an important feature is often muteness, though such children may speak in complete sentences on exceptional occasions.

It follows that there are three possible interpretations of such abnormal features as head banging, restlessness, destructiveness, peculiar movements, and screaming. In the first place, any one of these symptoms taken alone may be merely a passing phase in the life of a child and may have no serious significance. It may represent a natural reaction to some set of unfavourable circumstances such as a sudden alteration in the amount of parental attention available. Secondly, these symptoms may be the manifestation of a profound abnormality of personality in a childhood psychosis. In the present connexion I am using the term psychosis to cover a serious prolonged mental illness in which there is no evidence of gross organic brain damage and in which there is an impression of retention of a potentially normal mental capacity: fortunately such conditions are relatively rare in young children. Finally, these symptoms are by no means uncommon as part of the picture of simple mental defect.

At this point I would like to emphasize something which may be thought obvious—this is, that backward children, like ordinary children, react to their environment, though at a more infantile level. If that environment is conducive to the development of emotional disturbances then they may well develop and complicate the picture of straightforward defect. An investigation by Dr. M. Woodward (in press) showed that there was a correlation, significant at beyond the 0.001 level, between disturbed behaviour after admission to a mental deficiency hospital and a mentally adverse home background prior to admission, using objective criteria.

In order to illustrate the vexed question of infantile psychosis and mental defect a film was recently prepared by Dr. E. J. Anthony, of the Institute of Psychiatry, including some studies of typical mannerisms and movements. Two photographs illustrating this subject are reproduced here (Figs. 6 and 7) showing the mannerisms commonly seen in idiocy. Mannerisms of this type are described in such conditions as phenylketonuria, but they are in no way specific to this condition and may be seen in idiocy due to any cause. It is also very difficult to differentiate such mannerisms from those which may be seen in psychotic children. The distinction must be made on the basis of the general picture rather than of the individual symptom. In idiocy the child has not advanced beyond the level of repetitive manipulation, whilst in psychosis he may regress to that level. A clear history of previous normality is sometimes valuable in making the distinction, but there are reservations to this. In a minority of cases severe defect, perhaps amounting to idiocy, develops after some cerebral catastrophe—for example, post-inoculation encephalopathy or status epilepticus from whatever cause.

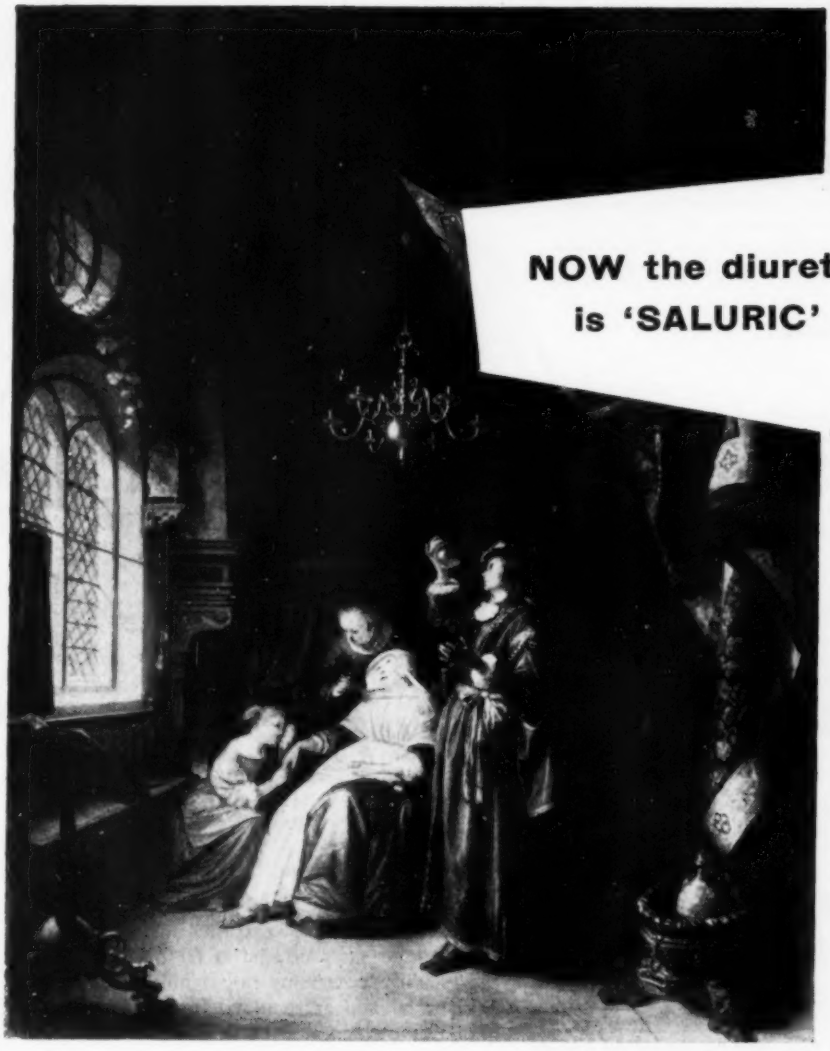
Limited Significance of Individual Features

It is extremely hazardous to make any definite forecast on the basis of a single defect or abnormality in the behaviour of a child. The question of mannerisms may be used to illustrate this point. Persistent head rolling is such a mannerism, and may be seen quite frequently in both idiot and psychotic children. It is also, however, by no means uncommon in normal children. It may, at one stage in the development of an otherwise quite normal child, seem to be an essential preliminary to sleep, when it appears to serve a self-hypnotic role. In normal children these circular activities of very limited scope tend to be broken as the child develops more complicated behaviour patterns and responds to a greater variety of stimuli. In idiots this does not happen, or happens only very slowly and as a result of intensive training. As with normal young children, idiots will tend to resort to repetitive self-hypnotic behaviour when there is little else to attract their attention or when they are bored. It is clear, then, that the presence of such a mannerism cannot in itself be the basis for a diagnosis of defect or of serious maladjustment.

FIG. 6.—This boy aged 10 years was thought to be normal up to the age of 3½ years but deteriorated rapidly. He now functions at imbecile level. He shows a variety of mannerisms.

Similar considerations apply to delay in any one accomplishment, though the reasons for this may be somewhat different from those which apply in the case of mannerisms. Urinary incontinence illustrates the problem very well. All young babies are incontinent of urine, as are most idiots, but it is well known that urinary incontinence, especially nocturnal, may persist into adult

FIG. 7.—An idiot aged 8 years suffering from phenylketonuria.



"La Femme Hydropique" (The Dropsical Woman) by Gerard Dou, painted in 1665. The original hangs in The Louvre.
Reproduced with acknowledgement to Archives Photographiques, Paris

Dropsy is a single sign but the causes are multiple.

When oedema is present, whatever the cause,

'SALURIC' is the diuretic of choice. 'SALURIC' orally,

replaces mersalyl and all other diuretics.

SALURIC *(Chlorothiazide)*

Chlorothiazide was discovered and developed in the Merck Sharp & Dohme Research Laboratories and is manufactured in England exclusively by the Merck Sharp & Dohme Organisation.

Full information is available on request.

How supplied: 'SALURIC' (Chlorothiazide) is supplied in 0·5 G. half-scored tablets in bottles of 100 and 500. The United Kingdom N.H.S. basic cost of an average week's treatment for a patient on maintenance therapy is 3/9d.

'Saluric' is a Regd. Trade Mark.

MERCK SHARP & DOHME LIMITED, HODDESDON, HERTFORDSHIRE MSD

New manufacturing technique brings significant increase in initial acid adsorption*

INTRODUCING DROXALIN GEL

Rapid adsorption of gastric hydrochloric acid is accepted as the most effective method of obtaining relief in peptic ulcer pain.

* In two minutes a single teaspoonful (3.5 mls.) of DROXALIN GEL will neutralise 50 mls. of N/10 HCl. This is *several times* the speed of acid adsorbents prepared by usual methods.

Using the well established Droxalin formulation a new and exclusive manufacturing technique has produced in DROXALIN GEL an antacid possessing this significant increase in initial acid adsorption. The advantages of quicker acting DROXALIN GEL in peptic ulcer therapy and hyperacidity will be readily recognised. The palatability of Droxalin Tablets is achieved.

DROXALIN Gel

ACID ADSORBENT

Droxalin palatability in liquid form

ACTIVE INGREDIENTS	DOSAGE	PACKS AND PRICE
Each teaspoonful (3.5 mls.) contains 60 grains Aluminium Hydroxide Gel B.P. (equivalent to 5 grains Dried Aluminium Hydroxide Gel B.P.) and 5 grains Magnesium Trisilicate B.P.	One or two teaspoonfuls one half-hour after meals. Repeat as necessary.	DROXALIN GEL is available in 8 oz. and 80 oz. bottles. Prescribable on E.C.10. Basic N.H.S. cost. 1/10d per 6oz. bottle.

CLINICAL TRIAL SAMPLES ON REQUEST TO :— SCOTT & TURNER LTD. NEWCASTLE UPON TYNE

life in a great variety of conditions apart from mental deficiency. A proportion of these cases are obviously neurotic in that they have other obvious features of neurosis, such as excessive anxiety, night terrors, shyness, timidity; others have some physical abnormality such as paraplegia to account for the weakness. In many children, however, this lack of sphincter control seems to be a solitary abnormality, and one is tempted to think in terms of delayed maturation of the apparatus responsible for the establishment of control. To base any far-reaching conclusions on the existence simply of urinary incontinence at, say, the age of 5 years is improper.

A word may also be said about the need for similar caution in interpreting normal behaviour in very young children. The older views about cerebral localization have come in for a good deal of criticism lately, and, while there is still a lack of general agreement on the subject, there is a tendency to a more dynamic concept of cerebral function which visualizes the central nervous system acting as a whole. None the less, it seems reasonable to suppose that activities such as breathing, coughing, and sucking, which are early developed, are more directly dependent on the integrity of the lower centres, while functions such as the use of logarithmic tables demand a certain amount of normal cortical tissue. The acquirement of skills such as sitting up independently and walking occupies an intermediate position. Most commonly, in severe mental defect the whole range of capabilities is affected in a fairly even manner. Even such elementary functions as coughing and swallowing may be seriously impaired, and breathing may be difficult to establish in a child with a severe brain abnormality. However, from time to time a case is encountered in which early development seems fairly normal in regard to the more vegetative functions and to early motor development. This may apply to children with a severe degree of tuberous sclerosis who may yet sit and walk at a normal time but prove eventually to be of idiot level. The most obvious explanation of this phenomenon would appear to be the fact that in severe mental defect there is a tendency for the higher centres to be more severely damaged than the lower. Similar considerations would apply to the case recently demonstrated by Professor Illingworth in which an infant with gross microcephaly passed the first "milestones" at the correct time.

A parallel with the phenomenon mentioned above may be found in cases of athetosis due to rhesus incompatibility. These children may seem fairly well after recovery from the acute illness (Crome *et al.*, 1955), and athetosis manifests itself only when the child reaches the stage of development at which co-ordinated purposeful movements are attempted.

Advantages and Disadvantages of Early Attention

I have avoided using the term "diagnosis" in this connexion, since mental defect is not a disease entity but rather a legal and social convention. As more light is thrown on the cause of deviation from the normal it becomes increasingly valuable to direct attention to young children who exhibit unusual or retarded behaviour. There is a small group of conditions which are amenable to direct treatment, such as cretinism, phenylketonuria, hypoglycaemia, galactosaemia. Some cases of petit mal associated with backwardness may also derive benefit from treatment. There is a whole group of children who are backward in certain respects whose prospects may be improved by careful study and advice. The most obvious of these is the group of deaf or partially deaf, but many other physical disabilities produce a similar effect. The deaf child is often regarded as mentally defective and frequently finds his way into a mental deficiency hospital, where he may develop a superimposed psychosis. It is essential that such a child should have expert advice and attention from an early age, and in his case the presenting symptom may be failure of speech development, inattention, and naughtiness, contrasting with a good level of attainment in some directions.

On the negative side, too much attention to delayed development at an early stage may distress the parent, may lead the doctor into unwise predictions, and may have a deleterious effect on the child's subsequent career. It is usually quite unjustifiable to ascertain a child under the age of 5 years as ineducable, and it is most undesirable that legal formalities such as certification as mentally defective should be undertaken at this stage. It is to be hoped that when new legislation is devised the present provision for the certification of young children as mentally defective will be replaced by a different arrangement for the care of such children, leaving it to the initiative of the parent to place them in hospital if this seems necessary. This should make it easier for the doctor to study the development and the needs of the individual child without the necessity to arrive at an early decision for purely statutory reasons.

Summary

It is seldom possible to predict accurately mental abnormality in a young child on the basis of specific behaviour disorders. Simple retardation of development is commoner than disturbed behaviour. In regard to mental deficiency it is possible to recognize only severe mental defect at an early stage. Often it is an adverse social background, not mental defect as such, which is the problem. Decisions regarding mental defect are often best postponed. The predictive value of tests under the age of 5 years is very low. A detailed history and physical examination are essential to assessment. Only 8% of 233 imbeciles and idiots drew their parents' attention by disturbed behaviour. The others were simply retarded. Disturbed behaviour of identical pattern may be found in idiots, in psychotic children, and, transiently, in normal children. The distinction must be based on the general picture, not on individual symptoms. Defectives are responsive to the environment and may develop a psychotic overlay in unfavourable circumstances. Even in severe defect early accomplishments are sometimes normal for the age. Early assessment and attention are important, especially where there are conditions which can be treated or complications such as deafness, but expediency should not be allowed to precipitate a rash decision which will prejudice the future of the child.

Permission has been received for reproduction of Fig. 1 from L. Crome and P. E. Sylvester's paper on hydrancephaly (*Arch. Dis. Childh.*, 1958, p. 235); of Figs. 2 and 3, from L. T. Hilliard and B. H. Kirman's *Mental Deficiency* (Churchill, London, 1957); and of Fig. 4 from I. Crome's article, "A Case of Lipoidosis Following Rh Factor Incompatibility" (*J. clin. Path.*, 1956, vol. 9, p. 326).

REFERENCES

Berry, R. J. A. (1938). *Cerebral Atlas of Normal and Defective Brains.* Oxford.
Craib, M. F., and Woodward, M. (1958). *J. ment. Sci.*, **104**, 115.
Crome, L. (1954). Ibid., **100**, 894.
—— Kirman, B. H., Marrs, M. (1955). *Brain*, **78**, 514.
Hilliard, L. T., and Kirman, B. H. (1957). *Mental Deficiency*, p. 224. Churchill, London.
Kirman, B. H. (1958). *J. ment. Sci.*, **104**, 167.
O'Connor, N., and Tizard, J. (1956). *The Social Problem of Mental Deficiency*, p. 37. Pergamon Press, London.
Vernon, P. E. (1955). *Bull. Brit. psych. Soc.*, **26**, 1.

The *International List of Advanced Programmes in Nursing Education*, published by the International Council of Nurses in 1954, has been brought up to date with the issue of a *Supplement*. This publication gives detailed information of programmes for "post-basic education of graduate nurses" in every country where such facilities exist. The *List* and *Supplement* can be obtained from the Council at 1, Dean Trench Street, London, S.W.1, price, post free, 21s. (*Supplement* only, 5s.).

SOCIAL WORK IN GENERAL PRACTICE

BY

MADGE DONGRAY, B.A., A.M.I.A.
Social Worker, Darbishire House Health Centre, University of Manchester

Considerable interest to-day is focused on the treatment and management of stress and strain and emotional disturbance in general practice. Opinions vary regarding the extent and importance of this problem, but few would deny that the family doctor, whether he likes it or not, is faced with a variety of social and emotional problems on which patients seek his advice and help. This raises the question of how far, in his capacity as medical adviser, he is concerned with them, and, if he feels rightly concerned, the question of what sort of help he can be expected to give. Here again opinions differ, ranging from the few doctors who consider these problems still outside their scope to those who consider the general practitioner should "do it all." The abundance of articles and correspondence on the subject, however, suggests that many family doctors feel a need for some sort of help in dealing with this aspect of their work, and some have written interesting accounts of the particular form of help they have chosen or have been able to find (Balint, 1957; Saville, 1957; Davis, 1957; Chalke and Fisher, 1957; Backett *et al.*, 1957).

At Darbishire House, Manchester University Health Centre, it was decided in June, 1955, for good or ill, to attach a trained social worker to the group of four family doctors practising from the centre and serving approximately 12,000 patients in a closely populated city area. I would like to say a little about this experiment.

First Steps

Experiment it certainly was, as the doctors had not worked directly with a social worker before and I had not worked in general practice. At the outset none of us had any clear idea of the sort of work which might be necessary or possible. The doctors knew that I had been a hospital almoner and had had some experience of child guidance, and it was agreed that in the first place they should refer to me any problems presenting social or emotional factors with which they thought or hoped I might be able to help.

During the first few months, which were largely spent in getting to know each other and learning to appreciate each other's points of view, two difficulties confronting the busy practitioner became steadily clearer; one was connected with the rapid advance in scientific medicine over the past 20 to 30 years, and the other with the growth of the social services over the same period of time.

The first difficulty is best illustrated by an account by one of the doctors of the tremendous change which the introduction of antibiotics had made in the management of pneumonia within his lifetime. Twenty years ago there was little the doctor could do but wait and hope until the crisis passed and then watch over a long, slow convalescence. Now the illness is usually arrested by a few injections, which take a minute or two to give and which can sometimes be delegated to the nurse. The relief from a heavy burden of responsibility in the doctor can readily be appreciated, but his personal contact with the patient and family is immeasurably curtailed and treatment tends to become a service rendered by the doctor rather than an experience lived through with the family. One suspects that the doctor may feel less helpless, but not the family. The mother who said, "We liked the old doctor; he used to *talk* to us about Johnny; the new one just sticks needles into him," was, I think, voicing her feeling that she no longer had any significant part to play in the treatment of her child. This does not, of course, mean that the new and the old approach cannot be combined, but perhaps they tend, at present, to remain distinct and are often kept so by the pressure of present-day practice and perhaps for other less obvious reasons.

The second difficulty concerns the rapid growth in the social services and revolution in social legislation over the same period of time. This often makes the doctor feel that management of his cases in a truly personal way has been taken out of his hands. With the best will in the world he could not be expected to be fully conversant with this side of the picture as well as keeping abreast of development in the medical sphere.

Thus doctors and patients alike tend to complain of a dwindling sense of responsibility and consideration towards each other in an age when pain and suffering are no longer accepted passively as the inevitable lot of man, and there is a general feeling that for any misfortune whatever there must be a remedy somewhere in somebody's hands.

Our experience at Darbishire House has, I think, shown that in both these spheres a social worker can give useful assistance to the doctor.

Using the Social Services Effectively

Part of the social worker's basic equipment is a sound knowledge of the social services, both statutory and voluntary. In addition it is her duty to know clearly how these services actually operate in the district in which she works, so that she can interpret and explain them to the doctor and patient, both of whom tend to find them confusing. She can then assist the doctor to choose the agency most likely to help his patient, and can also help him to prepare and assist the patient to make good use of the facilities offered.

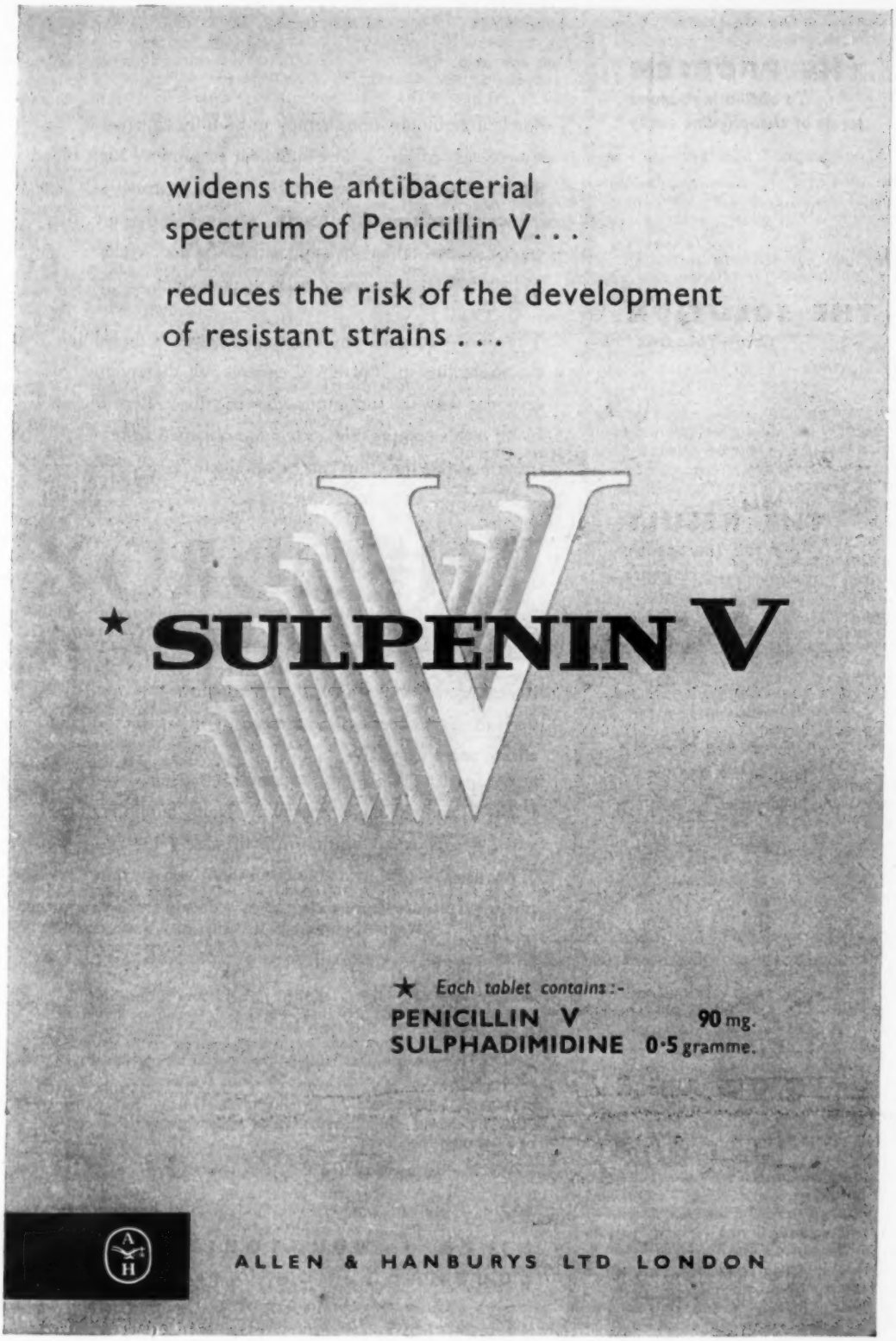
Take the simple example of advising a patient to attend a Ministry of Labour rehabilitation unit. It is important that the doctor distinguishes this service from Government training schemes, otherwise there is a danger of raising false expectations in the patient; it is useful to be able to answer some of the patient's questions about the allowances he will receive and to understand that he will not be guaranteed a job on completing the course, although the Ministry of Labour will do everything in its power to place him. It is helpful to understand the sort of experiences he may expect during the first few weeks at the unit: for the timid or truculent, for example, the aptitude tests can be a source of anxiety or irritation which may bring the patient back to complain at the surgery.

A patient who undertakes such a course free from avoidable misconceptions regarding its purposes is likely to make better use of the opportunity and to feel more confidence in the doctor who suggested it, and the social worker can often detect the hidden misconceptions which prevent patients from using the appropriate social service. For instance, a widow was found to be afraid to apply for National assistance because her husband had at one time drawn assistance under false pretences and she feared she would be penalized for his sins. A girl would not take out an affiliation order, believing that the court would send her to Borstal for having an illegitimate child while she was still under 21.

Doctors can attend lectures, read pamphlets, and pay visits of observation, but these time-consuming activities are, we think, no substitute for the opportunity to learn from repeated application and practice in collaboration with a social worker directly attached to the group.

Understanding Family Relationships

The social worker can often supplement the doctor's knowledge and understanding of family problems with her special skills in interviewing and understanding of personal


widens the antibacterial
spectrum of Penicillin V. . .
reduces the risk of the development
of resistant strains . . .
V
★ SULPENIN V
★ Each tablet contains:-
PENICILLIN V 90 mg.
SULPHADIMIDINE 0·5 gramme.
A H
ALLEN & HANBURYS LTD LONDON

THE PROBLEM

To obtain high blood levels of theophylline easily . . . For oral aminophylline therapy to be fully effective it is necessary to give a dose sufficient to produce high blood theophylline levels. However, because of gastric irritation vomiting often results. Alternative therapy with enteric coated tablets or suppositories is unreliable, and parenteral aminophylline is inconvenient.

THE SOLUTION

Oral 'Theodrox' . . . The combination of dried aluminium hydroxide gel and aminophylline in 'Theodrox' ensures full therapeutic response with the minimum of gastric upset. Reproduceable blood levels comparable with those obtained from intramuscular injection can be obtained.

THE RESULT

A full Therapeutic response . . .

THEODROX REGD.

Recent work[1,2] has shown that synthetic derivatives of theophylline are mostly unsatisfactory and all are more expensive.

Each 'Theodrox' tablet contains 3 grains aminophylline and 4 grains dried aluminium hydroxide gel. 'Theodrox' is also available combined with ⅛ grain phenobarbitone where a degree of sedation is also required.

REFERENCES

[1] *Brit. med. J.* (1957) *2*: 67

[2] *Ibid.*, page 74

DOSAGE . . .

ASTHMA:— two tablets, repeated in 2-3 hours if necessary to control paroxysm and dyspnœa. For prophylaxis, one tablet 4 times daily.

DIURETIC:— two tablets initially, then one or two tablets three times daily.

ANGINA PECTORIS:— four to eight tablets daily. In suitable cases 'Theodrox' with Phenobarbitone tablets can replace some or all of the 'Theodrox'.

PACKS:— Bottles of 25, 100 and 1,000 tablets.

RIKER

'Theodrox' (Brit. Pat. 727831) is a registered Trade Mark of

RIKER LABORATORIES LIMITED
LOUGHBOROUGH LEICS.

relationships. In an area such as ours it is not possible for the doctor to know all his patients and families intimately. Families move into and out of the district, split up, and come together again with surprising frequency. The doctor may be called suddenly to attend a family about which he knows nothing but where he senses underlying problems. Sometimes only one member of a family is registered with him, which makes it difficult to get a clear picture of the family as a whole; or the patient may be living alone, often as a result of intolerable conflicts with his family. In such cases an unhurried interview in which the patient does most of the talking and the social worker most of the listening, or a home visit to meet other members of the family, can illuminate the situation and enable the doctor to adopt the most helpful attitude towards the patient and family.

Young Mrs. X had been registered with the doctor for a few months, during which she had appeared repeatedly at the surgery seeking help with trivial ailments in herself and her baby daughter. The doctor was disturbed by her seemingly unreasonable demands on his time and patience, and asked me to see her.

She told a story of a grossly deprived and insecure childhood, and finished by saying, "The doctor is really a nice fatherly soul, isn't he?" This suggestion that she was seeking from the doctor a relationship which she had never had from her parents helped us to come to terms with our own attitude towards her.

Although her basic need for a good parent could never be fully satisfied by the doctor or anyone else, it was helpful that the doctor could understand this need and could tolerate and accept her demands without anxiety. It would have been no good to lecture her on being overanxious, but by accepting her anxiety as real and understandable he could give her a measure of reassurance and security which she should be able to communicate to her child, and, in a slight degree, prevent this child suffering as severely as she had done herself.

This sort of help may also be needed by families who have been registered with the doctor for some years and whose contact with him has been slight because they are seldom ill and send for him only in a crisis or because the management of the ill member of the family is in the hands of a hospital or other organization. This was the case with Mrs. Y, who had a spastic child, Jane, aged 2, and a normal healthy boy, John, aged 7 months. Mrs. Y had attended hospital regularly with Jane ever since she was a baby and also went to the child welfare centre with John, and she rarely sent for the family doctor. However, he was called in when John had bronchitis, and noticed that Mrs. Y spoke about Jane in such a way that he asked me to call and assess the situation, mentioning that the undesirable housing conditions made the problem of looking after Jane very difficult.

During my visit I gradually realized that Mrs. Y really had little idea of what to expect from Jane and did not seem to have grasped the implications of her condition. She held Jane up to show me her scissor gait, then put her on the floor, saying, "Look, she *won't* sit up." She put Jane in a chair with John, an extremely robust and vigorous child, and got annoyed with her for flopping over on to him. Mrs. Y was a young immature woman, but not by nature callous or unkind.

I discussed this with the doctor and suggested it would be helpful for someone to explain the child's condition to the mother and, if possible, to the father also, since Mrs. Y did not strike me as being capable of passing on to her husband, without distortion, whatever the doctor might tell her, and since any mother with a severely handicapped child needs the utmost support from her husband and this is more likely to be fostered by including him in consultations. Mrs. Y must certainly have received considerable information and advice already, but she had clearly been unable to accept and comprehend the nature of Jane's disability while she was still a baby, until John, at 7 months, had started to outstrip the 2-year-old Jane. It was then the family doctor to whom she voiced her anxiety.

The housing problem did undoubtedly add to her difficulties, but, in spite of application to the housing department, there was no hope of an early solution. However, after a long discussion with the doctor, Mr. and Mrs. Y thanked him for his help, and we learned a little later that they were saving a deposit for a new house.

Long-term Casework with Families

The foregoing examples mainly illustrate help I was able to give to the doctor; the next example is a little different in that the help was given more directly and continuously to the family.

Mrs. Z had been unfortunate with her children. After carrying her first baby eight months she was delivered of a macerated foetus; her second child, Paul, was a mongol; her third child, Douglas, developed epileptic fits at 2½. When I first met them Paul was 5 years old and attending an occupation centre daily; Douglas was 4, and Mrs. Z was complaining of his excessive temper tantrums and destructiveness.

During a visit to the home I saw both parents, who spent much time demonstrating to me, in the presence of Douglas, what a terrible child he was, with the natural result that he behaved accordingly. The mother was sure he was going to be delinquent; the father certain he was "mad" and would never allow his teachers to teach him anything if they succeeded in getting him to school at all. The father said, half provocatively, that friends had advised him to take the child to a psychiatrist, and the mother said that, although she had great faith in the doctor, they had never had "specialist" advice—she seemed to favour a medical or neurological consultation. In fact, the child's attacks were well controlled with phenytoin sodium and phenobarbitone, and he had only an occasional fit.

I suggested that, if the family doctor agreed, we could refer them to the psychiatric department of the children's hospital, where there was a close liaison with the neurological department. They were obviously in two minds about this, but agreed I should consult the doctor. From their manner it seemed to me that these two highly anxious, ill-informed, and guilty parents were unlikely to make good use of this offer without further help and encouragement. The mother poured scorn on those who had already attempted to help her with Paul, and the parents clearly felt threatened by the idea that anyone could do better with their children than they. On the other hand, I felt that behind all this display of aggressive anxiety was considerable positive feeling.

A report was sent to the hospital, and, pending an appointment, I visited the mother fortnightly, seeing her for about an hour. At first she was aggressively casual, but on the third visit this attitude collapsed as she told me how difficult it was to be the mother of the only two children in the street who were "queer"—how she felt people criticized her for being too severe or too lenient with them, making her feel she ought not to have had them at all or should have put them in a home. Gradually she was able to discuss her wish to reject her children and her guilt about it, as well as her wish to cherish them, and how both she and her husband wondered why this had happened to them and who was to blame. She had rather resentfully given up work when Douglas started having fits and had taken to minding three normal children under 3 years of age from 8 a.m. to 5 p.m. five days a week in a house which was barely big enough to hold her own family. She denied emphatically that Douglas could feel jealous of these children, although he was often aggressive towards them; nor could she admit any rivalry between Douglas and Paul, as "she treated them both alike although Paul was worth ten of Douglas." Gradually, however, she began to watch Douglas's behaviour towards the other children and to admit its meaning; and she also began to realize that it was impossible

to treat a mongol child and an intelligent epileptic one exactly alike and to see that it must be difficult for Douglas to have an older brother who will remain a baby while he has to grow up.

Mrs. Z attended the psychiatric department in due course and obtained some satisfaction from learning that Douglas was of normal intelligence and some measure of reassurance about handling his tantrums and understanding of his type of epilepsy. She would not agree to attend more regularly than at three-monthly intervals, and, after consultation with the psychiatrist and his social worker, I continued to visit the home, extending the intervals between interviews as the situation improved.

The family was helped to tackle its housing problem, and there is a definite hope of removal within 18 months. This seems to have spurred the father on to get a better job, but the mother has begun to talk about loneliness on a new estate. Facing a new set of neighbours may well arouse some of her old fears, so we will try to keep in touch with her for a while round the removal time.

It is not possible to give an account of all that has been discussed or has happened during the 12-months association with this family, but certain changes have occurred: medication for Douglas has been reduced and he has not had a fit for nine months; and he started school recently without undue disturbance.

The precise reasons for these changes are open to dispute, although this is not the only case in which a gradual reduction in the need for medication has followed a combined attempt by the doctor and social worker to understand the emotional stresses in a family in which the patient has been diagnosed as having epilepsy. The situation is by no means stable even now, but the mother often speaks of Douglas as "really a very good boy" and the relationship between them seems calmer and warmer. We have yet to see if the improvement will last, as my visits become less frequent and we cannot definitely claim to have prevented more serious and chronic trouble later, although, judging from the accounts we often hear about the distressing early experiences of adult epileptics with disturbed personalities whose families do not appear to have had similar help, we hope that some lasting benefit has been given in this case.

The tensions in this family had been building up for a long time—at least from the shock of Mrs. Z's first disastrous pregnancy. The problem centred in feelings of failure and inadequacy in having produced three damaged children—an extremely difficult situation for any couple to face, much less Mr. and Mrs. Z, who had themselves both suffered considerable emotional deprivation in their own childhood. Many workers had attempted to help them piecemeal with these problems, but what the family most seemed to need was a steady relationship with one person who could accept and tolerate the situation at its most explosive and encourage them to talk freely without fear of criticism or coercion; someone, moreover, who could act as a focusing point, helping them to integrate the separate experiences with the doctor, psychiatrist, health visitor, and teacher, and with relatives and neighbours.

This sort of relationship, I suggest, could not have been supplied by the doctor even though the problem in this case was directly associated with medical care, but it was most appropriately handled by someone working in close co-operation with the doctor.

Conclusions

In conclusion I would like to summarize some advantages which appear to belong particularly to a setting in which a social worker is attached directly and exclusively to a group of family doctors.

1. Accessibility

Help is available on the spot whenever the doctor is puzzled or disturbed by a particular problem, and consequently he tends to seek it more readily than if this were to involve considerable time and effort in seeking it elsewhere. This is particularly so where the problem does not fall easily into a case for referral to any of the well-known social agencies, but where the dominant need is for an assessment of the situation on which to base a plan of help.

2. Participation in Group Discussion

Informal group discussion over morning coffee will often centre in a particular patient or family; more often it will concern the wider aspects of social care such as housing or employment policy, care of handicapped children or old people, or such perennial points of dispute as "malingering," use and abuse of the Health Service, the "unreasonable" patient, the "problem" family. The social worker can often bring a fresh perspective to bear on these subjects or provide information in the light of which judgments can be confirmed or modified.

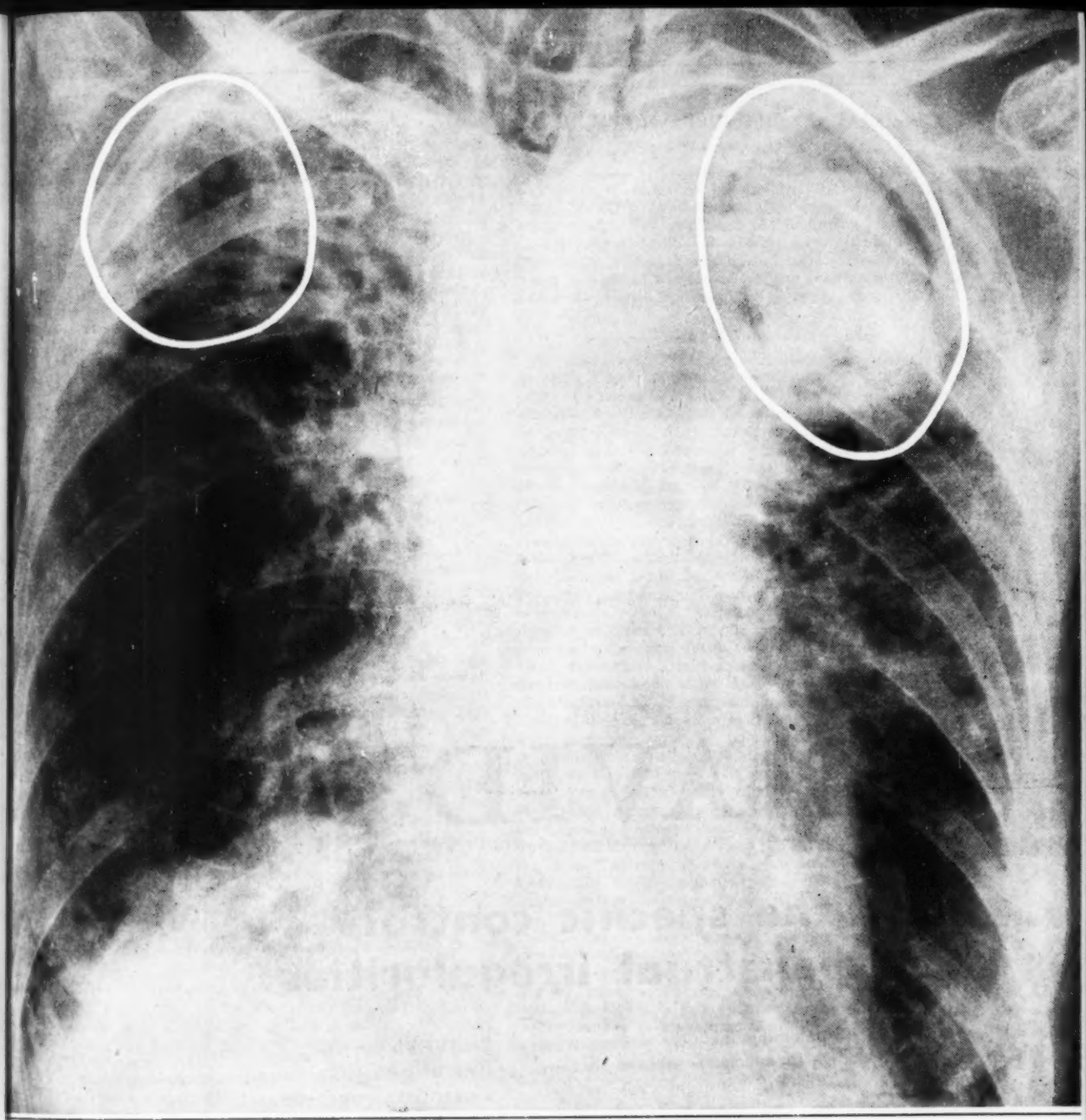
3. Interpretation of the Aims and Limitations of Social Work

During the early months of my appointment the attitude of the doctors to me (as a social worker and not as a person) swung from scepticism about the value of social work in general to completely unrealistic demands on my resources. My own feelings were naturally coloured by the anxiety of working in a new setting, but it seemed to me that I was expected as "a nice motherly soul" to perform miracles which the psychiatrist had failed to produce; as a "strong right arm" to the doctor to wrest from the authorities houses for all the ill-housed, jobs for all the unemployed; as an "expert" to clean up and re-educate problem families of long standing; in short, to relieve the doctor of all those painful situations in which he felt unable to be effective in his own right. Those who complain most loudly that social workers spoon-feed their clients and sap their sources of self-help and initiative sometimes demand just this from workers with whom they come in contact.

It was only gradually that we saw that the doctor and social worker must pool their resources and think about their work together in terms of the achievement of reasonable expectations and limited aims. We had to distinguish between what the doctor and social worker might want and what the patient wanted; to examine the values and principles which guided our work and to ask whether disappointing results arose from inadequacies within ourselves, the families, or the social system, or from factors about which we still have little knowledge. To cure sometimes, to relieve often, and to comfort always could then be accepted as applicable to social work as it is to medicine. The more realistic conception of social work aims and methods achieved through daily discussion and experiment can then be transferred to the relationship between the doctor and other social workers outside the group whom the doctor may wish to contact on his own initiative.

4. Exploration of the Role of the Social Worker as Colleague of the Doctor

Patients who consult the doctor on social or emotional problems or who present symptoms which appear to be connected with such difficulties may, I think, be said to have chosen the doctor as a source of help rather than anyone else. They are therefore likely to have strong feelings about any attempt on the doctor's part to suggest they look elsewhere for aid even though they may clearly be asking for the sort of assistance the doctor does not feel qualified to give. If the doctor's own conception of social work is not clear he will hesitate to redirect his patients but remain uneasy at being unable to help them. To have acquired an informed attitude towards social work as described in the last section is therefore helpful, but the strength of the patients' feeling towards the doctor has also to be reckoned with. Too hasty a referral to the social worker may be interpreted as a rejection, and we have learned from experience that it is only when the patient feels assured that the doctor has taken his trouble seriously that he can



Long-standing tuberculosis in a woman of 65.
Left: large tuberculous solid area overgrown with Aspergillus.
Right: large cavity not blocked.

THERAPAS. The original Calcium B-P.A.S.
Now widely used as a preferable alternative to P.A.S. Minimises gastro-intestinal upset: virtually tasteless.

Whenever Calcium B-P.A.S. is indicated specify

THERAPAS

A PRODUCT OF

Smith & Nephew *Pharmaceuticals* Limited

SPECIALISTS IN TUBERCULOSTATIC DRUGS

to treat a mongol child and an intelligent epileptic one exactly alike and to see that it must be difficult for Douglas to have an older brother who will remain a baby while he has to grow up.

Mrs. Z attended the psychiatric department in due course and obtained some satisfaction from learning that Douglas was of normal intelligence and some measure of reassurance about handling his tantrums and understanding of his type of epilepsy. She would not agree to attend more regularly than at three-monthly intervals, and, after consultation with the psychiatrist and his social worker, I continued to visit the home, extending the intervals between interviews as the situation improved.

The family was helped to tackle its housing problem, and there is a definite hope of removal within 18 months. This seems to have spurred the father on to get a better job, but the mother has begun to talk about loneliness on a new estate. Facing a new set of neighbours may well arouse some of her old fears, so we will try to keep in touch with her for a while round the removal time.

It is not possible to give an account of all that has been discussed or has happened during the 12-months association with this family, but certain changes have occurred: medication for Douglas has been reduced and he has not had a fit for nine months; and he started school recently without undue disturbance.

The precise reasons for these changes are open to dispute, although this is not the only case in which a gradual reduction in the need for medication has followed a combined attempt by the doctor and social worker to understand the emotional stresses in a family in which the patient has been diagnosed as having epilepsy. The situation is by no means stable even now, but the mother often speaks of Douglas as "really a very good boy" and the relationship between them seems calmer and warmer. We have yet to see if the improvement will last, as my visits become less frequent and we cannot definitely claim to have prevented more serious and chronic trouble later, although, judging from the accounts we often hear about the distressing early experiences of adult epileptics with disturbed personalities whose families do not appear to have had similar help, we hope that some lasting benefit has been given in this case.

The tensions in this family had been building up for a long time—at least from the shock of Mrs. Z's first disastrous pregnancy. The problem centred in feelings of failure and inadequacy in having produced three damaged children—an extremely difficult situation for any couple to face, much less Mr. and Mrs. Z, who had themselves both suffered considerable emotional deprivation in their own childhood. Many workers had attempted to help them piecemeal with these problems, but what the family most seemed to need was a steady relationship with one person who could accept and tolerate the situation at its most explosive and encourage them to talk freely without fear of criticism or coercion; someone, moreover, who could act as a focusing point, helping them to integrate the separate experiences with the doctor, psychiatrist, health visitor, and teacher, and with relatives and neighbours.

This sort of relationship, I suggest, could not have been supplied by the doctor even though the problem in this case was directly associated with medical care, but it was most appropriately handled by someone working in close co-operation with the doctor.

Conclusions

In conclusion I would like to summarize some advantages which appear to belong particularly to a setting in which a social worker is attached directly and exclusively to a group of family doctors.

1. Accessibility

Help is available on the spot whenever the doctor is puzzled or disturbed by a particular problem, and consequently he tends to seek it more readily than if this were to involve considerable time and effort in seeking it elsewhere. This is particularly so where the problem does not fall easily into a case for referral to any of the well-known social agencies, but where the dominant need is for an assessment of the situation on which to base a plan of help.

2. Participation in Group Discussion

Informal group discussion over morning coffee will often centre in a particular patient or family; more often it will concern the wider aspects of social care such as housing or employment policy, care of handicapped children or old people, or such perennial points of dispute as "malingering," use and abuse of the Health Service, the "unreasonable" patient, the "problem" family. The social worker can often bring a fresh perspective to bear on these subjects or provide information in the light of which judgments can be confirmed or modified.

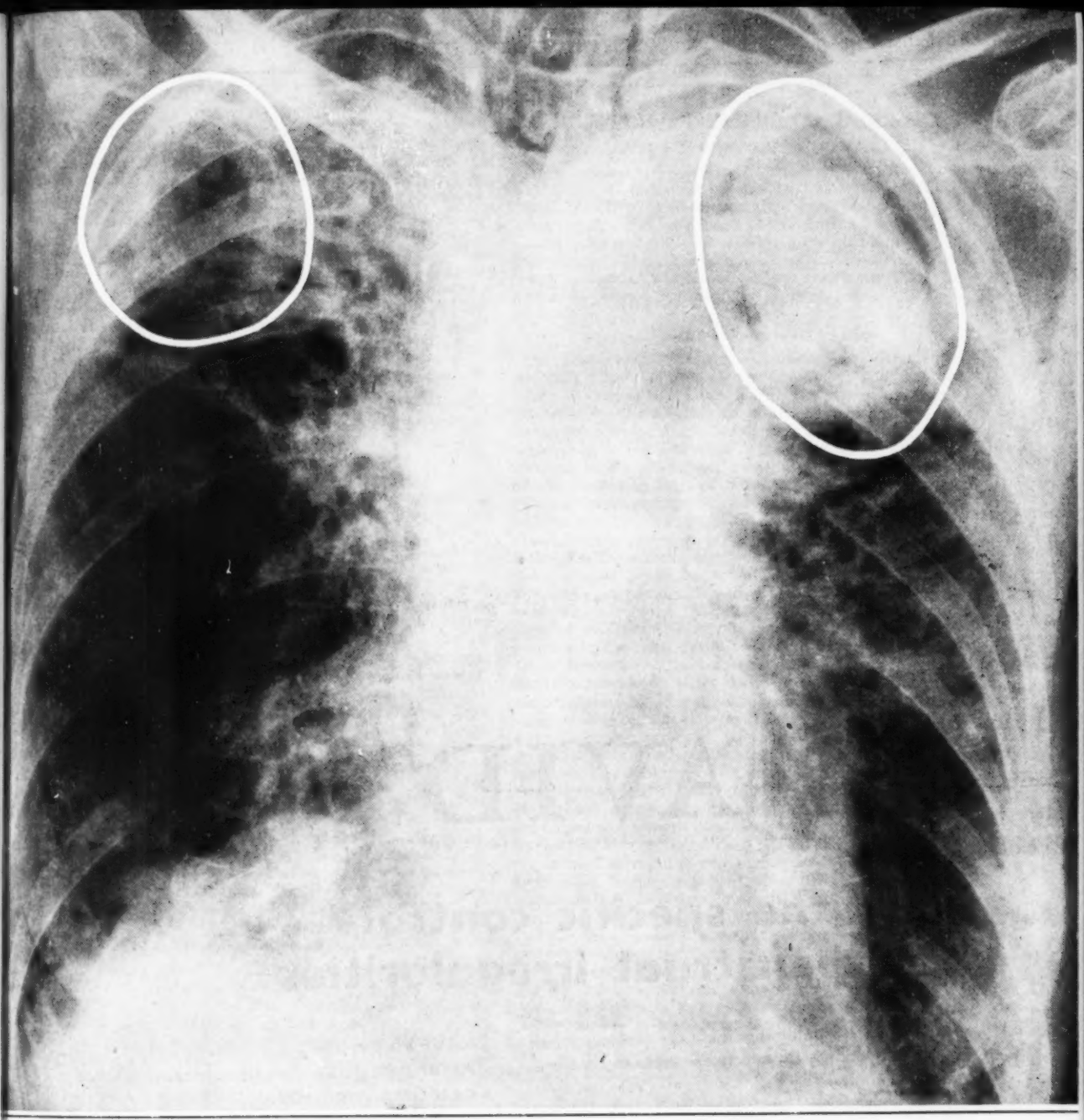
3. Interpretation of the Aims and Limitations of Social Work

During the early months of my appointment the attitude of the doctors to me (as a social worker and not as a person) swung from scepticism about the value of social work in general to completely unrealistic demands on my resources. My own feelings were naturally coloured by the anxiety of working in a new setting, but it seemed to me that I was expected as "a nice motherly soul" to perform miracles which the psychiatrist had failed to produce; as a "strong right arm" to the doctor to wrest from the authorities houses for all the ill-housed, jobs for all the unemployed; as an "expert" to clean up and re-educate problem families of long standing; in short, to relieve the doctor of all those painful situations in which he felt unable to be effective in his own right. Those who complain most loudly that social workers spoon-feed their clients and sap their sources of self-help and initiative sometimes demand just this from workers with whom they come in contact.

It was only gradually that we saw that the doctor and social worker must pool their resources and think about their work together in terms of the achievement of reasonable expectations and limited aims. We had to distinguish between what the doctor and social worker might want and what the patient wanted; to examine the values and principles which guided our work and to ask whether disappointing results arose from inadequacies within ourselves, the families, or the social system, or from factors about which we still have little knowledge. To cure sometimes, to relieve often, and to comfort always could then be accepted as applicable to social work as it is to medicine. The more realistic conception of social work aims and methods achieved through daily discussion and experiment can then be transferred to the relationship between the doctor and other social workers outside the group whom the doctor may wish to contact on his own initiative.

4. Exploration of the Role of the Social Worker as Colleague of the Doctor

Patients who consult the doctor on social or emotional problems or who present symptoms which appear to be connected with such difficulties may, I think, be said to have chosen the doctor as a source of help rather than anyone else. They are therefore likely to have strong feelings about any attempt on the doctor's part to suggest they look elsewhere for aid even though they may clearly be asking for the sort of assistance the doctor does not feel qualified to give. If the doctor's own conception of social work is not clear he will hesitate to redirect his patients but remain uneasy at being unable to help them. To have acquired an informed attitude towards social work as described in the last section is therefore helpful, but the strength of the patients' feeling towards the doctor has also to be reckoned with. Too hasty a referral to the social worker may be interpreted as a rejection, and we have learned from experience that it is only when the patient feels assured that the doctor has taken his trouble seriously that he can



Long-standing tuberculosis in a woman of 65.
Left: large tuberculous solid area overgrown with Aspergillus.
Right: large cavity not blocked.

THERAPAS. The original Calcium B-P.A.S.
Now widely used as a preferable alternative to P.A.S. Minimises gastro-intestinal upset: virtually tasteless.

Whenever Calcium B-P.A.S. is indicated specify

THERAPAS

A PRODUCT OF

Smith & Nephew *Pharmaceuticals* Limited

SPECIALISTS IN TUBERCULOSTATIC DRUGS

ENAVID*

BRAND OF NORETHYNODREL AND ETHYNYLOESTRADIOL 3-METHYL ETHER

For the specific control of menstrual irregularities

ENAVID, containing the new Searle steroid norethynodrel, permits *specific* and usually complete *control* of the menstrual cycle on *oral* administration and thus provides effective therapy for most menstrual irregularities.

ENAVID has strong progestational and a lesser oestrogenic activity on the endometrium, which stimulates its development to a secretory phase. It also inhibits the secretion of gonadotropins by the anterior pituitary gland.

ENAVID is therefore recommended for:

- **AMENORRHOEA** (Primary and Secondary)
- **OLIGOMENORRHOEA**
- **MENORRHAGIA**
- **METRORRHAGIA**
- **DYSMENORRHOEA**
- **PREMENSTRUAL TENSION** and the
- **"INADEQUATE LUTEAL PHASE"**

ENAVID is supplied as 10 mg. tablets in bottles of 20 and 50 tablets.

Detailed literature is available on request.

* *Trade Mark.*

SEARLE

G. D. SEARLE & CO., LTD., HIGH WYCOMBE, BUCKS. Tel. High Wycombe 1770

EN : P117

tolerate the idea of discussing it with someone else, whom the doctor can then introduce as a colleague, supplementing and not supplanting the aid he offers. In other words, the social worker becomes a sort of extension of the doctor, and patients are then able to accept her as an integral part of the service.

The patient's loyalty almost inevitably remains with the doctor. I well remember the slight shock I experienced when a patient whose problem had been satisfactorily resolved said to me, "the old 'Doc' worked jolly hard on that problem"—my own contribution had been apparently incidental. Our close association has made both the doctors and me very much more aware of the feeling content of the doctor–patient relationship and consequently able to use it more effectively.

5. Discovering Unmet Need in General Practice

It has been shown from the examples quoted in this article that some of the patients and families were already in touch with other workers. Mrs. Y, for example, was known to the staff at the welfare clinic, to the specialist, the physiotherapist, and possibly the almoner at the hospital; Mrs. Z was being visited at intervals of three to six months by the health visitor responsible for the care of children under 5 and by another who supervised the baby-minding; she was also known to the school health and education department in respect of the mongol child. The needs of the family as a whole, however, had either not been recognized by the other workers, each of whom gave particular help with particular problems, or, if they were recognized, it had not been possible, for one reason or another, for them to give the overall help needed. Particularly in the case of Mrs. Z there was a need for one person to undertake the job of standing alongside the family, co-ordinating their experiences in seeking help with their problem; and this sort of need appears to us to occur more often than suspected in general practice. This was also recognized during a survey of a general practice carried out by the Social Medicine Research Unit of the Medical Research Council in 1953 (Backett *et al.*, 1954). "This is not just a question of better co-ordination of the services . . . the need is for a person, someone with professional training and skill, who can help people by means of a casework relationship to use their own and the community's resources in tackling their problem" (Shaw, 1954).

6. Opportunities for Preventive Work

The family doctor is often in a unique position for observing the earliest signs of social and emotional breakdown. Particularly in the case of mothers and babies, he witnesses early signs of anxiety and stress which, left unrelieved, may have serious repercussions in their emotional development and future happiness. Each time the doctor and social worker collaborate in analysing and assessing family needs and tensions the importance of relieving early signs of stress becomes more apparent. Until recently, at any rate, social workers have been made more aware of this in their training than medical students in theirs, but I think it is clear from the examples quoted here that unless *both* the doctor and the social worker appreciate the importance of this aspect of family care on equal terms little can be achieved.

Hence, for the time being at least, there is much to be said in favour of providing the general practitioner with an opportunity of working with a social worker in closer relationship than has hitherto been the custom.

References

Backett, E. M., Heady, J. A., and Evans, J. C. G. (1954). *Brit. med. J.*, **1**, 109.
—— Maybin, R. P., and Dudgeon, Y. (1957). *Lancet*, **1**, 37.
Balint, M. (1957). *Brit. med. J.*, **1**, 156.
Chalke, H. D., and Fisher, M. (1957). *Lancet*, **2**, 685.
Davis, N. (1957). Ibid., **1**, 160.
Saville, P. R. (1957). *Brit. med. J.*, **1**, 158.
Shaw, L. A. (1954). "The Need for Social Casework in the Setting of a General Practice." *Case Conference*, vol. 1, No. 5.

RHEUMATIC DISEASE AND INDUSTRY

[From a Special Correspondent]

A joint meeting of the Empire Rheumatism Council and the Association of Industrial Medical Officers was held at the Royal Society of Medicine on October 30 as part of the latter society's 84th meeting. The Chairman, Dr. W. S. C. Copeman, opening the discussion, drew attention to the importance of the rheumatic diseases in industry. This group of diseases was second only to respiratory illness as a cause of absence from work.

Field Surveys

Professor J. H. Kellgren, director of the Rheumatism Research Centre of Manchester University, said that the study of rheumatic diseases had in the past been greatly hampered by the lack of diagnostic definitions—from the eighteenth-century belief that most musculo-skeletal pains were gouty to the nineteenth-century concept of rheumatic fever as an all-embracing rheumatic process. Two recent developments had been of the greatest importance here—radiology and serology. Radiology had enabled rheumatoid arthritis to be distinguished from what he preferred to call osteoarthrosis; and, later, other polyarthritides such as spondylitis, Reiter's disease, and psoriatic arthropathy had come to be defined. Serological work had shown that rheumatoid arthritis is associated with a macro-globulin which appeared to be specific, and that this might be associated with visceral, vascular, and cutaneous manifestations of the disease. Biochemical techniques might well add further knowledge. These developments had enabled field workers to gather accurate information about the prevalence and incidence of various forms of chronic rheumatic disease. Professor Kellgren then described the procedure used in some of these surveys, emphasizing the difficulties of relying on only clinical diagnostic criteria. Many of these difficulties did not arise in radiological and serological studies. Radiological surveys had the advantage that standardization could be achieved, observer-error studies could be carried out, and the films could be kept as a permanent record. Serological studies had also produced results of great value. He cited the familial aggregation of the rheumatoid serum factor as an example, and suggested that this might be analogous to the hyperuricaemia of gout. From the epidemiological standpoint there were two main groups—those with the generalized changes of osteoarthrosis and disk generation, the most important numerically, and, secondly, those with inflammatory polyarthritis. For both of these groups we now had the techniques and equipment to study them in industry. Interesting variations in prevalence had already been noted—for example, as between rural and urban populations in South Wales.

Dr. J. S. Lawrence, director of the Empire Rheumatism Council's mobile field unit, said that industry was concerned not only with direct environmental factors but also with absenteeism due to rheumatic diseases generally. With an ageing population the latter would become increasingly important. He quoted National Health Insurance statistics for 1953–4, which showed an annual loss of 28 million man-days from rheumatic disease alone. After reviewing the role of the rheumatic diseases in various industries, he described a survey designed to investigate the prevalence of rheumatism in miners. This showed a clear association between the severity of *x*-ray changes in the lumbar spine and the complaint rate of back–hip–sciatic pain. A further survey had then been conducted to study possible occupational factors, and this had shown an association with back strain, other postural factors, and exposure to damp conditions. He believed that the heavy toll of rheumatic disease in miners was largely preventable, mainly by increased mechanization, which need not, as it was inclined to do at present, involve the use of still heavier equipment. Turning to rheumatoid arthritis, he said there were evidently considerable regional differences. This disease affected 3.3%

of adults in Leigh, Lancashire, but only 2% in Pittsburg, U.S.A. These differences became even more marked after correction for the different age-structures of the population. Dr. Lawrence had also studied the value of routine physiotherapeutic measures in the treatment of rheumatic disease, and produced data to show that recovery could be hastened quite appreciably and rendered more complete by appropriate physiotherapy, active and sometimes passive movements and heat being of value, but massage appearing to have no detectable effect on recovery rates.

Variants of Rheumatoid Arthritis

Professor E. G. L. BYWATERS, director of the Medical Research Council's special unit for juvenile rheumatism, then discussed unusual variants of rheumatoid arthritis. The definition of the usual in a disease of unknown aetiology was difficult enough, and, although dogmatic criteria could be and indeed had been agreed upon, many cases fell into the "probable" and "possible" categories. The variant might be hard to distinguish, especially at the onset, even in those cases which eventually developed all the classical features of the disease.

He then went on to describe some of the more unusual presentations of rheumatoid arthritis, including those that began with involvement of a particular joint such as in the big toe, which were often labelled as "gout"; those with fever, pericarditis, and a migratory polyarthritis, mislabelled "rheumatic fever"; cases which remained limited to one particular joint for a long period of time, usually treated as tuberculous unless the clinician was aware that rheumatoid arthritis not infrequently presents in a single joint. The disease might be confined to bursae and tendon sheaths, in the foot producing "metatarsalgia," or oedema without obvious joint involvement; palindromic rheumatism, with recurrent attacks of pain and swelling in numerous joints over many years, each lasting about 24 hours and then returning completely to normal. These were illustrated by a series of cases, as was the so-called "anarthritic" rheumatoid arthritis. Finally he mentioned cases presenting with iritis, pericarditis, or as a pyrexia of unknown origin. They should be on guard against regarding this disease—or any disease—as a real entity; by providing a specific name we implied that a disease had as much real existence as an elephant or a giraffe. Rheumatoid arthritis should be thought of as a reaction pattern to perhaps a number of different factors. Study of the variants might eventually give some clue to the nature of these factors.

QUEEN MOTHER AT KING'S

Paying her first visit to King's College Hospital since becoming Chancellor of London University, QUEEN ELIZABETH THE QUEEN MOTHER opened a new extension to the Medical School on November 4. One of the pleasures of being Chancellor, she said, was that it brought her frequently into touch with institutions with which she was already familiar. The University's medical ramifications were a constant source of interest, and she had noticed particularly that association with the University, especially in the case of the medical schools, did not mean dull uniformity: each school had its own individuality based on the history and traditions of which it was rightly proud. It might be, however, that with the passage of time some traditions became less important. For example, the liberal attitude which King's had adopted towards the admission of women medical students was no longer distinctive, since all the other medical schools in London had followed suit.

No one could predict what the future held, but it was wise of the School to put its house in order and to see that its facilities for teaching and research kept pace with the ever-increasing demands that were likely to be made upon them. It was from this point of view that the new extension was so timely. "I wish," she added, "there was in sight an equally satisfactory solution to that great problem which faces both the Hospital and the School: the need for more beds."

In his address of welcome to Her Majesty, the chairman of the Medical School, Mr. R. A. HORNBY, said the reason why it had been necessary to add to the buildings of a medical school which had no present intention of increasing its students was that, with the advance of medical science, it was essential to provide accommodation and equipment to keep pace with it.

Dr. VERNON F. HALL, dean of the School, said the total costs of the extension had been some £205,000, of which well over half had been generously contributed by the University Grants Committee. The remainder had been found from the School's own funds, including a bequest by Dr. Harold Wiltshire, a former member of the staff. The extension housed the new medical and surgical units and a considerable addition to the department of chemical pathology; there was a large practical pathology classroom and a clinical lecture theatre designed for showing cases to small groups of students. The other facilities included a clinicopathological demonstration room in which all aspects of selected diseases could be displayed for varying periods, accommodation for the Clubs and Societies Union, a mixed common room for students, and a council room. Unfortunately, it had not been possible to establish a chair in medicine as there were not sufficient beds to satisfy the needs of a professorial unit, but part-time directorships had been established in medicine and surgery. The medical unit was under the direction of Dr. Clifford Hoyle, and the new surgical unit under Mr. Harold Edwards. The extension to the department of chemical pathology provided a suite of nine research laboratories which would be a valuable addition to Professor C. H. Gray's overflowing department.

Her Majesty then inspected the new building and unveiled a plaque commemorating her visit.

HEBERDEN SOCIETY

At a meeting of the Society at Stoke Mandeville Hospital on October 11 Dr. M. SAXTY GOOD reviewed his series of 20 patients with temporal arteritis. Headache had been a prominent feature in every case; tender and thickened temporal arteries in 19; constitutional illness, anorexia, and fever in 16; pain and stiffness of the jaws in 9; painful neck in 9; and pains in the muscles and limbs in 10. Twelve had developed eye involvement, of whom three not treated with cortisone had become suddenly blind. The average duration of disease after biopsy in the patients not receiving steroids and in eight patients receiving steroids was 5.4 and 2.5 months respectively. His experience and that of others suggested that early biopsy for diagnosis, followed by cortisone treatment, could shorten the disease and prevent blindness.

Dr. A. R. HORLER and Dr. MALCOLM THOMPSON (Newcastle) had found instances of pleural effusion complicating rheumatoid arthritis in 8 out of 52 men and one out of 128 women, as against only one in 180 control patients without this disease. In 5 men the pleural effusion was an inaugural event in the development of the arthritis. Dr. C. J. BARFORD (London) reported the case of a woman with rheumatoid arthritis who developed fever and pericarditis and a positive L.E.-cell test after five years of prednisolone therapy. She also had unusual nodules at the lung bases, which proved to be tuberculous at necropsy.

New Steroids

Dr. H. F. WEST (Sheffield) opened a discussion on the new steroids triamcinolone and dexamethasone. Twenty-eight patients with rheumatoid arthritis on prednisolone were allocated at random either to continue with this steroid or to change to triamcinolone, on a roughly "tablet-for-tablet" basis. Those who changed had fared slightly but not significantly better, but the average dose (9 mg.) of triam-

(*Continued at foot of next page*)

To-day's Drugs

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Dolviran (Farbenfabriken Bayer A.G.; distributors, Levmedic Ltd.).—Each tablet contains acetylsalicylic acid 0.2 g., phenacetin 0.2 g., codeine phosphate 0.01 g., caffeine 0.05 g., phenobarbitone 0.025 g. The valuable analgesic effects of combinations of aspirin, phenacetin, and codeine are well known. Caffeine is a stimulant of the central nervous system and phenobarbitone is a depressant of the central nervous system. It would seem to be illogical to prescribe them together. The quantity of caffeine in this preparation, however, would have a negligible effect, as it is about a third of what would be contained in a small cup of tea. This preparation is about three times as expensive as compound codeine tablets *B.P.*

N.H.S. basic price : 10 tabs., 2s. 2d.

Robaxin (A. H. Robins Co. Ltd.)—This is 2-hydroxy-3-*o*-methoxyphenoxypropyl carbamate (methocarbamol), and is one of the derivatives of mephenesin which have been tested in an attempt to find a more effective drug for the relief of skeletal muscle spasm. It has a more prolonged action than mephenesin and has been reported to be effective in treating acute muscle spasm associated with injuries and orthopaedic conditions, but is of only limited use in treating spasticity and rigidity caused by lesions of the central nervous system. It often causes slight drowsiness and dizziness, but serious toxic effects have not been reported. It is supplied in tablets of 0.5 g., and the dose suggested by the makers is 4–9 g. daily, depending on the severity of the spasm.

N.H.S. basic price : 50 tabs., 21s. 8d.

(*Continued from previous page*)

cinolone was probably on the high side and was apt to produce excessive side-effects. In another group of patients steroid hypertension was not altered by change to triamcinolone. The new drug had been useful to some patients who were excessively wakeful on prednisolone, but its tendency to reduce appetite and cause loss of weight and weakness was a disadvantage. Other speakers reported that triamcinolone caused excessive loss of muscle tissue in some patients, giving the clinical appearance of a myopathy. Experience of dexamethasone was limited, but it seemed an effective drug. Caution was needed, since it had been reported that dexamethasone could suppress the adrenal cortex in sub-therapeutic doses, a finding so far not confirmed.

Dr. J. F. BUCHAN (London) had treated 38 ambulatory patients suffering from rheumatoid arthritis with chloroquine sulphate. In a double-blind trial, objective assessment of disease activity and joint involvement at three and six months showed chloroquine sulphate to be clearly, but weakly, effective in this disease. Stainable bone-marrow iron had been studied by Drs. A. G. S. HILL and C. L. GREENBURY (Stoke Mandeville). It proved to be absent or scanty in 56%, and excessive in 22%, of 120 patients with rheumatoid arthritis, but there was no correlation with circulating haemoglobin. Remissions of disease induced by steroids were accompanied by rise of haemoglobin and disappearance of excess concentration of marrow iron. Dr. J. J. R. DUTHIE (Edinburgh) had confirmed that large doses of intravenous iron (up to 5 g.) induced remission in a controlled trial in rheumatoid arthritis. As part of the remission there was an improvement in the accompanying anaemia. Dr. W. R. M. ALEXANDER (Edinburgh) described experiments in purifying the rheumatoid agglutinating factor.

Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Iproniazid Jaundice

SIR,—The three articles concerning the toxic effects of iproniazid ("marsilid") (*Journal*, November 1, pp. 1067, 1068, and 1070) are valuable. In view of the reports that iproniazid administration is sometimes associated with jaundice, this case report of a patient who received iproniazid 100 mg. daily for five months and died from hepatic coma may be of interest.

Miss C. Y., aged 70, attended the department of cardiology, Edinburgh Royal Infirmary, as an out-patient on March 11, 1957, because of effort angina of nine months' duration. Although there was no clinical history of myocardial infarction, an electrocardiogram showed old transmural posterior and anteroseptal myocardial infarcts. Glyceryl trinitrate and restriction of her activities were advised. She was next seen one year later on March 13, 1958, at a routine follow-up clinic, when it was noted that her angina was less incapacitating and that she was able to walk half a mile (0.8 km.) without stopping. In April her family doctor prescribed iproniazid 50 mg. twice daily, with subsequent reduction of the incidence of angina and of her requirement of glyceryl trinitrate from 8 to 1 or 2 tablets of 1/130 gr. (0.5 mg.) daily.

On August 8, 1958, her sister noticed that her conversation was muddled and that she was slightly confused. She complained of vague ill-health, and two days later visited her family doctor, who noticed that she was slightly jaundiced and discontinued iproniazid. Her confusion continued, and during the night of August 14 she was found wandering in the garden of her house, shouting and disorientated. On the evening of the following day she was admitted as a certified patient to a mental hospital. Jaundice was present and there was tenderness in the right hypochondrium. Her confusion fluctuated until the third day after admission, when she became semicomatose and deeply jaundiced.

She was then admitted to the Edinburgh Royal Infirmary under the charge of Dr. Rae Gilchrist on August 18. Jaundice was marked. There was no history of any contact with infective hepatitis or of any venepuncture as a possible source of homologous serum jaundice. There was guarding in the right hypochondrium, but no detectable hepatic enlargement. There was no splenic enlargement or ascites. Temp. 97° F. (36.1° C.), pulse 70, resp. 18, B.P. 110/60, Hb 97%, W.B.C. 5,300, E.S.R. 6 mm./hr. The urine contained bile and urobilinogen. Serum bilirubin 6.3 mg.%, alkaline phosphatase 19 K.-A. units, zinc and thymol turbidity 8 units each. Serum sodium 128 mEq/l., serum potassium 3.54 mEq/l., serum chlorides 105 mEq/l. Prothrombin activity 36%. Blood urea nitrogen 19 mg.%. Total proteins 5.8 g.%. Electrophoresis of serum proteins showed that 45% was albumin, 8% alpha$_1$-globulin, 7% alpha$_2$-globulin, 10% globulin, and 30% gamma-globulin. The patient became progressively more disorientated and required paraldehyde for sedation. Incontinence developed after three days. Serial liver function tests showed little significant change. She was treated with intravenous 5% glucose saline or 50% glucose with added potassium chloride. Her serum potassium and sodium were controlled at a steady level until the eleventh day, when her serum potassium dropped to 2.76 mEq/l., from 3.34 mEq/l. Despite the administration of more potassium chloride, her serum level remained low and was 2.76 mEq/l. when she died in coma on September 5.

At necropsy, the liver was flabby and slightly smaller than normal (1,070 g.). Its capsule was normal and on section the parenchyma was soft, diffluent, and brownish yellow. The intrahepatic bile ducts showed no macroscopic abnormality. The gallbladder contained concentrated bile and was normal. The common bile duct was patent and healthy. Histological examination revealed subacute and extensive necrosis of the liver: the lobular pattern was partly destroyed and large numbers of polymorphs and round cells were present in the bile ducts and periportal tissue. The heart showed left ventricular hypertrophy and the myocardium had marked focal fibrosis with widespread patchy necrosis. Although the coronary ostia was patent, the whole coronary arterial tree was markedly involved with atheroma

It cannot be said that this patient died from hepatic coma as a result of iproniazid therapy, but no other cause for her jaundice and liver damage was evident.—We are, etc.,

Rosslynlee Mental Hospital, Midlothian. J. D. W. FISHER.
Royal Infirmary, Edinburgh. M. F. OLIVER.

Aspirin and Gastro-intestinal Haemorrhage

SIR,—The article by Dr. L. Th. F. L. Stubbé (*Journal*, November 1, p. 1062) showing the loss of occult blood after administration of aspirin is alarming when related to the vast quantities of aspirin consumed by the general public. These results are supported by the work of Dr. W. H. J. Summerskill and Dr. A. S. Alvarez published the same week in the *Lancet* (November 1, pp. 920 and 925). Not only will these results make the consideration of all salicylic therapy a necessity, but raise questions outside the direct control of the medical profession. Prescribing may be controlled, but what of the vast consumption by public purchase, and the false idea of safety? Should not control be exercised? It is realized that aspirin may not be placed on the Poisons List, but manufacturers should at least be made to include a warning on their packings. Is there no method of legislation to enforce this?—I am, etc.,

Guy's Hospital, London, S.E.1. JOHN DOBBING.

SIR,—Having come pretty near death in my time from a bleeding duodenal ulcer, after taking aspirin for incidental headaches, I do not need to be convinced that aspirin makes ulcers bleed. But Dr. L. Th. F. L. Stubbé, in his most interesting paper (*Journal*, November 1, p. 1062), shows that taking aspirin regularly for a week or so will make even a normal volunteer lose more than 4 ml. of blood a day from his intestinal tract in two-thirds of cases. This seems to prove that it is dangerous to take a couple of aspirins three times a day for chronic painful conditions, such as "rheumatism." It looks as if some other analgesic, or coated tablets of sodium salicylate, will have to be tried in such patients.

But it would surely be a pity if Dr. Stubbé's admirable bit of work was applied to taking occasional doses of aspirin for headaches, etc. This is about the most effective of our "bathroom cupboard" analgesics and hitherto has seemed as safe as its nearest rival—a double whisky. Even if two or three aspirins do turn out to cause gastric hyperaemia and consequent oozing of blood from the gastric or intestinal mucosa, provided this occurs only once in a while, need one bother much? Because, as you will recall, the second figure in Douthwaite and Lintott's paper[1] on the gastroscopic findings after aspirin was an illustration of the effect of a single dose of mustard, as taken with beef steak. And their fine colour photographs demonstrated convincingly that, though chunks of aspirin produced a localized hyperaemia, the mustard produced a more generalized and at least equally intense gastric reaction.

Before frightening the public into giving up their favourite home remedy for occasional familiar pains, should we not warn them that their taste for condiments is probably quite as dangerous? Or can we be reassuring on the present findings, provided, as always, that they practise moderation?—I am, etc.,

Tonbridge. E. CLAYTON-JONES.

REFERENCE

1 Douthwaite, A. H., and Lintott, G. A. M., *Lancet*, 1938, **2**, 1222.

Antibiotic Therapy for Bronchitis

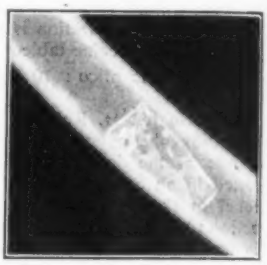
SIR,—I read with interest the article on continuous antibiotic therapy for adult chronic bronchitis by Drs. Gordon Edwards and E. C. Fear (*Journal*, October 25, p. 1010). This is a very common ailment especially here in the North, and already "this season" I have treated chronic bronchitics for their more acute relapses. I was therefore delighted to see how the treatment as advocated in the article gave such significant relief. But the sting comes at the end—the cost of the tetracyclines was £45–£55.

In these days of very necessary awareness of costs, what am I to do? If I treat, say, only a few of the many bronchitics in this practice, the costing department of the Ministry of Health will not look upon me with favour. The fact that I am possibly saving expenditure in other Ministries does not interest them, neither does the fact that the patient continues working throughout the winter show in any Ministerial estimates. A hospital bed not used sounds a weak argument to account for above-average prescribing. My moral obligation to the patient is to help his discomfort and improve his prognosis. I would be grateful for guidance in this problem.—I am, etc.,

Wilmslow, Cheshire. A. H. LUSCOMBE.

Foreign Body in Endotracheal Tube

SIR,—I wish to record a rather unusual case of respiratory obstruction during endotracheal anaesthesia. The patient was anaesthetized and intubated with a large Portex endotracheal tube. He immediately showed signs of respiratory obstruction. Manual squeezing of the reservoir bag was met by resistance, and produced no expansion of the chest. Laryngoscopy showed no obvious cause of obstruction, so the endotracheal tube was removed with immediate relief, thus confirming the advice, "Respiratory obstruction can be relieved by the simple expedient of withdrawing the tube and giving the patient a chance to breathe normally."[1]



On examination of the tube the lumen was found to be completely obstructed by a cork. The radiograph shows the cork *in situ* outlined with barium. A similar cause of obstruction has recently been described.[2]—I am, etc.,

The Royal Infirmary, Cardiff. K. A. STEWART.

REFERENCES

1 Macintosh, R. R., Mushin, W. W., and Epstein, H. G., *Physics for the Anaesthetist*, 2nd edition, p. 269. Blackwell Scientific Publications.
2 Haselhuhn, D. H., *Anaesthesiology*, 1958, **19**, 561.

Hydrocortisone for Asthma

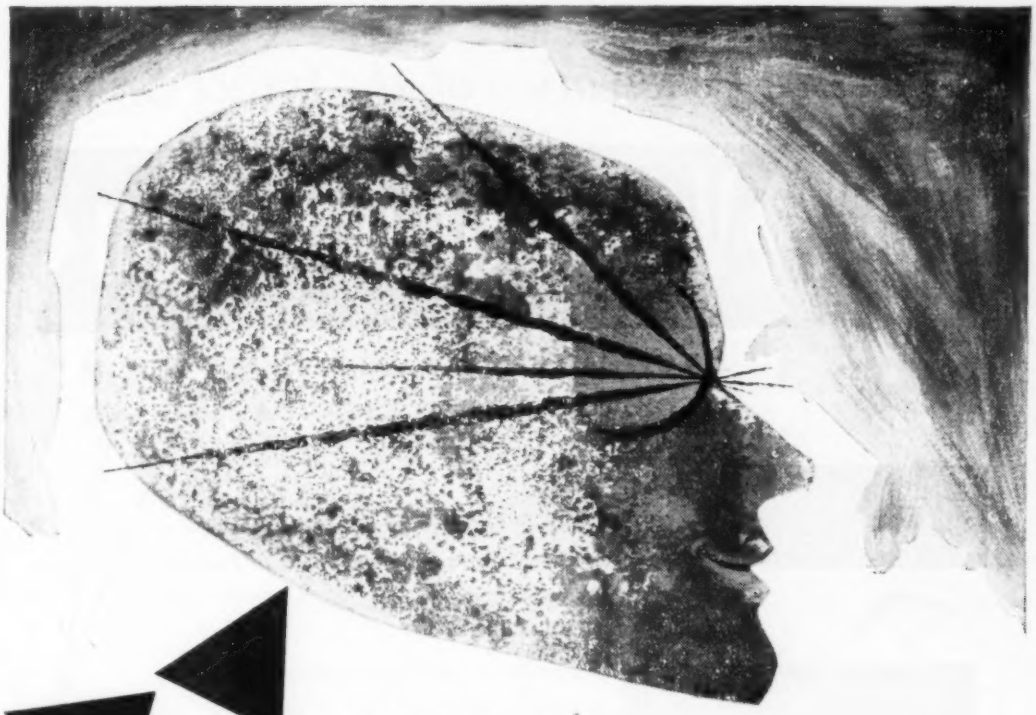
SIR,—In the *Journal* of September 27 three papers dealing with the hydrocortisone treatment of bronchial asthma[1-3] describe methods we introduced several years ago in our department.[3 4]

We administered prednisone powder+lactose by nasal and oral insufflation and hydrocortisone solution by oral spray. The first method we tried on asthmatics with rhinitis and tracheobronchitis, using double-blind control groups of lactose and quinine insufflations. The results were checked by relief of symptoms. The treatment was successful in cases where rhinitis predominated. In hydrocortisone inhalation therapy the presence of blocking mucus in the bronchi and bronchioli presented the greatest problem. We worked out a method of sucking this mucus by a double catheter introduced into the trachea as far as the bifurcation; the suction was achieved by electric apparatus.

After this preliminary treatment patients inhaled a solution containing 50–150 turbidity-reducing units of hyaluronidase ("hyason") and 25 mg. hydrocortisone ("hydroadreson"). The hyaluronidase facilitates the absorption of hydrocortisone on the mucous membrane. We continued this treatment twice weekly, giving 3–30 treatments per case, depending on the severity of the asthmatic state. About 300 cases of asthma have been treated in the past four years.

We controlled our cases by serial determinations of 17-ketosteroid excretion and vital capacity. We found that removal of mucus, hyaluronidase, or hydrocortisone spray alone caused neither a significant rise of vital capacity nor of 17-ketosteroid secretion, but 3–6 combined treatments had a marked effect.

For treatment we selected cases of severe intractable asthma, gaining a good response in 50–60%. Patients with secondary complications (emphysema, cor pulmonale, bronchiectasis) did not respond well, whilst infective agents were eliminated by simultaneous penicillin–streptomycin inhalation.



for mild sedation
with nutritional support

The debilitated patient, whether recovering from severe illness or operation or suffering from a chronic disease, is greatly benefited by the addition of nutritionally generous supplements of vitamins of the B complex and ascorbic acid. Such patients often need also mild sedation.

A combination of the necessary vitamins with a relatively low dose of phenobarbitone is now available as Tropenal.

Tropenal

FORMULA

Each tablet contains

Aneurine hydrochloride B.P.	5 mg.
Riboflavine B.P.	5 mg.
Pyridoxine B.P.C.	2 mg.
Nicotinamide B.P.	15 mg.
Ascorbic acid B.P. ..	50 mg.
Phenobarbitone B.P. ..	16 mg. (¼ gr.)

In designing the formula, it was necessary to bear in mind the known antagonism between barbiturates and the vitamins of the B complex, together with the theoretical possibility that the effects might cancel each other out. But preliminary trials have shown that on account of the varying speeds of action and other factors not fully understood, the combination is clinically effective.

INDICATIONS

(1) Anxiety states with restlessness, especially associated with hypertension, alcoholic withdrawal or peptic ulcer.

(2) Progressive illness in which insomnia is associated with a need for the greatest nutritional support—e.g. congestive heart disease, cachectic states.

(3) During convalescence, to speed recovery by promoting good appetite and a quiet frame of mind associated with nutritional adequacy.

(4) Insomnia not induced by pain.

DOSAGE

One to four tablets daily.
Tablets in packs of 100 and 500.

Standard Reference Cards.

Factual information on all our products is available. Produced in accordance with A.B.P.I. Specifications, cards can be obtained from our representatives or from Vitamins Ltd.

VITAMINS LIMITED (DEPT. A.3.) UPPER MALL, LONDON, W.6.

Effective Penetration of the Intact Skin

Vascutonex Cream

A TOPICAL SALICYLATE THERAPY WHICH INCORPORATES TWO ESSENTIAL FACTORS

Effective skin penetration

Effective absorption into lipid tissue

The first factor is provided by diethylamine salicylate, which has been shown to have an absorption rate 300–500 times greater than methyl salicylate.*

The second factor is glycol salicylate, the slow release of which from fatty tissue prolongs the action of the quicker acting diethylamine salicylate.

The local effect of these salicylates is to begin their therapeutic action at the site of the lesion. By plain inunction, about 80% of the salicylate content of the cream is taken up into the body and about 60% is excreted in the urine.

VASCUTONEX is non-staining, odourless, and contains no counter-irritants — its therapeutic action depending entirely on the effective absorption and anti-rheumatic action of the salicylates in the formula.

INDICATIONS: Fibrositis and pain associated with muscular and articular rheumatism and all soft tissue pain.

* *Comptes rend. Soc. de Biol.*, 1948, **142**, 819.

Formula
Glycol Salicylate . . . 10% w/w
Diethylamine Salicylate . . . 10% w/w
in a water miscible base.
Pack: 30 gramme tube.
Basic N.H.S. cost: 2/6d. plus P.T.

CALMIC LIMITED · Crewe: Crewe 3251-7
London: *2 Mansfield Street W1 · Langham 8038-9*

The advantages of inhalation or insufflation therapy consist in the more economic use of hydrocortisone and in minimizing side-effects (salt and water retention, adrenal atrophy), thus necessitating neither special precautions nor salt-free diet. Severe cases had to be treated with additional short-term administration of prednisone or corticotrophin (orally and/or parenterally) and antispasmodic inhalation. Our combined method is an improvement on the treatments described in the above-mentioned articles,[1 2] in so far as it deals with the mucus obstruction and makes local hydrocortisone therapy accessible in a wider field of asthmatic cases.—I am, etc.,

Budapest, Hungary. M. K. HAJÓS.

REFERENCES

1 Herxheimer, H., McAllen, M. K., and Williams, D. A., *Brit. med. J.*, 1958, **2**, 762.
2 Helm, W. H., and Heyworth, F., ibid., 1958, **2**, 765 and 768.
3 Hajós, K., *Allergie u. Asthma*, 1956, **2**, 363.
4 —— *Acta allergol. (Kbh.)*, 1958, **12**, Suppl. 5.

Thiopentone Convulsion?

SIR,—Thiopentone-twitching is seen from time to time even after adequate premedication. The present case, a big man of 47 years of age, was given promethazine and pethidine, 50 mg. of each intramuscularly 90 minutes preoperatively. On arrival in the anaesthetic room he was asleep, though not soundly asleep. Shortly after the administration of 0.5 g. of thiopentone sodium as a 5% solution into the lateral vein of the antecubital fossa of the left arm, the left forearm and hand began to "convulse." The right arm, both legs, and face were unaffected. The "convulsion" passed off in about 20 seconds or so. There was no respiratory spasm whatever.

The nature of the movements was interesting. Flexion and extension at the elbow, combined with pronation and supination, predominated; the thumb was in moderate opposition, and the fingers developed a strange type of wave of metacarpophalangeal flexion passing from the second to the fifth joints and then being repeated fairly rapidly. I was extremely interested in this phenomenon, though not, perhaps surprisingly, the least bit alarmed, for the patient had warned me that he would do just this. "I have done this before just as I am going off. You see I am a fireman, and it is second nature for me to reach to the knob and turn on extra oxygen via the bypass. As I have no apparatus on, I shall try and search for it." And this explanation satisfied me completely.—I am, etc.,

Barnet General Hospital, Herts. ERIC K. GARDNER.

Buzzers for Bed-wetters

SIR,—The dramatic effectiveness of this method of curing nocturnal enuresis in many children is of considerable physiological interest. At first sight it is difficult to see how the bell can be effective when it rings *after* the event. However, modern knowledge of the central nervous system indicates that afferent stimuli reach the brain in vast numbers day and night. These are all extinguished in a few seconds unless something arouses attention to them. If attention is aroused immediately after an event, it seems possible to recover memory of events a few seconds prior to alerting. Thus a deep sleeper may know that it was a sound that wakened him if he becomes alert within a few seconds. Similarly the bell of the buzzer may call up a memory of a bladder sensation a few moments before, and may thus lead to an association in the brain between this bladder sensation and a disturbing noise—hence the cure. It seems surprising to me that anyone should think this method is psychologically harmful, for if properly staged the whole treatment becomes a harmless game. In some cases there are psychological problems, but they are often more the result than the cause of enuresis. In any case cure should surely come first and any psychotherapy of patient and parents come second, if this is still required.—I am, etc.,

Department of Neurology, United Oxford Hospitals. W. RITCHIE RUSSELL.

Prevention of Lung Cancer

SIR,—Dr. G. B. Forbes (*Journal*, November 1, p. 1104) disagrees with Mr. Leslie J. Temple's suggestion (*Journal*, October 4, p. 858) that the coroner should be notified of deaths due to carcinoma of the lung in heavy smokers because there is no significant occupational or industrial link as with pneumoconiosis or mule-spinners' cancer. He goes on to point out that not all heavy smokers develop cancer of the lung and that non-smokers sometimes do. But surely not all exposed workers develop pneumoconiosis or mule-spinners' cancer; such absolute standards as he seems to require regarding smoking as a cause of death are neither logical nor necessary. If in the doctor's opinion death is due primarily to smoking, he is entitled to say so on the death certificate and it is then for the coroner to decide what action he will take. The coroner in the Southwark inquest of October 29 is reported (*Daily Mirror*, October 30) as saying that the inquest was held because the Registrar of Deaths had formed the opinion from the certificate that the circumstances were similar to those which applied when a person died from cirrhosis of the liver caused by alcohol, a view apparently accepted by the coroner himself. There is therefore no necessity to postulate an industrial or occupational cause.

Furthermore, the coroner is reported as saying, "If Dr. (Paul Frederick) Lister had been content to say that death was 'due to smoking,' nobody would have quarrelled with him." If the newspaper reports are correct, this is a most important declaration, implying acceptance of the contention that the prime cause of death in smokers who have died from cancer of the lung is what we in fact believe it to be—namely, the smoking of tobacco. The position now would seem to be that if a doctor believes his patient died as a result of smoking he is not only entitled to say so on the death certificate but that ethically he should say so; it is not a question of making the coroner's court a platform for propaganda but a straightforward issue as to what it is right and proper to do.—We are, etc.,

Stanmore, Middlesex. NORMAN MACDONALD.
London, W.1. WILFRED LESTER.

Appendicitis in the Aged

SIR,—In his letter Dr. J. A. H. Lee (*Journal*, October 25, p. 1039) presents some interesting statistics. My attention was attracted to the fact that whilst the death rate from appendicitis in the age group 80–84 has hardly changed since 1937–8, the death rates in the age group 60–64 have dropped by two-thirds for men and three-quarters for women. It would be interesting to compare the incidence of the disease, in these age groups during the same period, with the mortality rates, for then I think it would be possible to show whether Dr. Lee's first or second postulated mechanism accounted most for the change—i.e., whether less people are developing the disease, or whether treatment has improved.

In support of Dr. Lee's third postulated mechanism, Dr. Erik Christensen's paper (*Journal*, October 4, p. 832) shows that older people are more likely to develop gangrene and perforation without alarming symptoms, so that the rate of complications and the mortality rate are raised.—I am, etc.,

Scarborough Hospital, Yorks. CHARLES A. PRICE.

Breast-feeding

SIR,—Dr. Bruno Gans's article (*Journal*, October 4, p. 830) is one of many dealing with breast-feeding that assume that mothers who do not breast-feed are in need of attention and that their attitude arises from unfortunate circumstances. A "good" reason for not breast-feeding is pain, but other reasons are grouped under "emotional, domestic, or economic," all of which exclude a thought-out attitude on the part of the mother. Most articles seem to take this approach, although a case has been argued against the superiority of breast-feeding—e.g., the recent survey in

Middleton, Lancashire.[1] One day an article might be written where some mothers' refusal to breast-feed is attributed to a belief that artificial feeding is just as beneficial with fewer side-effects. My wife's experience, having her first baby earlier this year at University College Hospital, London, was a very pleasant one. At the antenatal clinic and in hospital she stated her views in favour of artificial feeding. After some discussion her views were respected and no breast-feeding occurred at all. In some hospitals this would be unheard of, but I feel they would do well to follow suit.—I am, etc.,

LEO GOLDSTONE,
Statistician, Essex County Council.

Chelmsford.

REFERENCE

[1] Burns, C., *Med. Offr.*, 1957, **98**, 205.

Thoracic Outlet Compression Syndrome

SIR,—The case histories of two patients under my care whose cervical ribs and upper dorsal ganglia had been removed for symptoms of arterial occlusion in the fingers make me less optimistic that these procedures will prevent the progress of the disease than Professor G. C. Rob and Mr. A. Standeven appear to indicate in their article on the complications of the thoracic outlet syndrome (*Journal*, September 20, p. 709). A further patient whom I have recently treated for blockage of the first part of the subclavian artery, and hope to describe in detail, presented with symptoms which previously would have been ascribed to compression of the artery at the thoracic outlet. The Seldinger technique of aortography permits demonstration of the branches of the aortic arch with minimal upset and danger to the patient. I suggest that until the patency of the appropriate vessels at their origin has been proven by aortography peripheral external pressure of any kind ought not to be considered as a cause of abnormal vascular symptoms and signs in one upper limb.

Case 1.—Female: At the age of 32, 1946, for three months attacks of numbness and whiteness in left ring and middle finger when cold. Rounded pulsatile swelling above left clavicle. Left radial pulse abolished when shoulders braced back and arms raised above head. Thick tendinous scalenus anticus divided and cervical or anomalous first rib removed, and two months later upper dorsal ganglionectomy was performed by Sir James Learmonth because frequent vasospastic attacks persisted in the hand. Relief was temporary but the condition not disabling until 1957, when a sudden attack of pain in the whole arm, forearm, and hand, together with coldness and weakness, occurred. No major pulse was now palpable distal to the bifurcation of the brachial artery. The aneurysm which Sir James had found at the first operation starting behind the lateral border of the scalenus anticus was excised.

Case 2.—Female: At the age of 21, 1957, pain and colour changes in the left hand were produced by cold. A left cervical rib was removed in Galway, but the symptoms persisted and were relieved by upper dorsal sympathectomy performed by Professor P. A. Fitzgerald a year later. Sympathectomy for similar symptoms appearing in the right hand and feet in 1952 was similarly successful (H. S. S.). In 1956 the patient suffered pain in the left forearm and hand of sufficient severity to prevent her working. The hand was pale and the radial pulse absent. An aortogram by the Seldinger method showed blockage of the second part of the subclavian artery with some filling of the axillary artery. Treatment by thromboendarterectomy or insertion of a bypass graft is contemplated.

Case 3.—Female: At the age of 46, 1956, small patches of superficial venous thrombus occurred and resolved on the left upper limb. Pain and colour changes in the fingers of the left hand when cold for eighteen months. Persistent pain and early gangrene of finger-tips for six months. Thrill and bruit over left subclavian artery, radial pulse present. Blood pressure—right arm 180/95 mm. Hg: left arm 140/75 mm. Hg. Aortogram showed incomplete blockage of the first part of the left subclavian artery. Thromboendarterectomy of the first part of the subclavian artery, the occluding plaque being removed by direct arteriotomy after exposure of the area by resecting the left fourth rib. All pain was relieved, normal blood pressure was restored, and the gangrene is resolving.

—I am, etc.,

H. S. SHUCKSMITH.

Leeds, 1.

Antibiotics in Acute Tonsillitis and Otitis Media

SIR,—I was extremely interested in Dr. John Fry's contribution (*Journal*, October 11, p. 883) on the use of antibiotics in acute tonsillitis and acute otitis media. It is of the greatest interest to see the "opinions" which many of us have formed from "impressions" checked in this way by a general practitioner in a scientific manner.

I should be very glad if Dr. Fry could check another impression which I have formed, quite without scientific corroboration—namely, that recurrences of acute tonsillitis and acute otitis media occur more frequently in those patients who are given penicillin at the first onset of the illness than in those who receive no antibiotics. I have delayed or withheld penicillin in the treatment of many cases of acute tonsillitis, particularly in children, in recent years (unless other reasons for giving it were present), believing that the untreated patient can build up an immunity.—I am, etc.,

M. BARROW.

Birmingham, 14.

Halothane Concentration

SIR,—Please allow us to comment on some points raised by Drs. P. J. C. Burton and F. R. Gusterson (*Journal*, September 27, p. 799).

(1) It is stated that the Coxeter-Mushin Mark I unit is unsuitable for use with closed-circuit halothane because of "relatively large areas of dead space." This statement simply does not make sense. There can be no dead space in a circle system save that between the system and the patient's alveoli. A moment's reflection will show that the charge of gases in the system is moved onward with each respiration of the patient, and that in the Coxeter-Mushin unit each inspiration supplies the patient with a gas mixture which has passed twice through the carbon-dioxide absorber and once (in part) through the halothane vaporizer, irrespective of the contained volume of the system. We have had Coxeter-Mushin units (both Mark I and Mark II) in daily use with halothane for nearly a year and can detect no difference in the clinical results obtained.

(2) The writers state, "Work is in progress which will demonstrate clearly . . . that, in a true circle system with halothane, the carbon dioxide build-up with low minute volumes is very slight and of no clinical significance." Surely this forecast of results before the completion and publication of research can only cast doubts upon the impartiality with which the work is being carried out, thus bringing to naught the laudable desire of Drs. Burton and Gusterson to further the use of closed-circuit halothane.

(3) Drs. Burton and Gusterson are "perturbed . . . that an anaesthetist might be content these days to use an unknown concentration of halothane." We on the other hand are perturbed to find anaesthetists of their experience so obsessed with mathematical symbols. Surely it must be clear by now that the only reliable indication of vapour strength of any inhalation anaesthetic in clinical use is the condition of the patient. In closed circuit anaesthesia far too many variable factors affect the concentration of the anaesthetic vapour to allow of any accurate calibration by percentage, and, as for fabricating a vaporizer to deliver a "safe" concentration of halothane, we believe that no vaporizer has any clinical application unless it can deliver a vapour strong enough to produce third plane anaesthesia in the most resistant patient. Administration of such a concentration to a feeble emaciated individual would quickly produce respiratory arrest. For which type of patient is the projected "safe" vaporizer to be calibrated?

(4) Drs. Burton and Gusterson refer to our recently published articles[1] as authority for the statement that halothane is certain to ruin the ether vaporizer of the B.O.C. circle unit. They seem to have misunderstood our statements. If they will reread the articles in question we hope it will become quite clear to them: (*a*) That only the Boyle II machine in its present form is temporarily "ruined" by halothane. The lesion produced is "gumming" of the vaporizer drum caused by combination of the lubricant with metallic salts formed by the action of halothane on the alloy of which the machine is made. The resultant thick paste prevents movements of the control drum. (*b*) That the Coxeter-Mushin machines can be easily and rapidly fitted with plastic washers and gaskets which make them absolutely halothane resistant. We have had about a year's trouble-free service from four such units in this hospital group.

(5) The great danger of sudden increases in vapour concentration is described when B.O.C. circle units are used with halothane.

We can only say that in a series of some 2,000 cases using the circle absorber units of the Coxeter-Mushin (Marks I and II) and the Boyle II machines we have encountered no such danger in any case. In our experience each setting of the vaporizer control produces a fixed stable level of anaesthesia in a given patient. This level can be maintained hour after hour once the appropriate setting has been found to suit both patient and surgeon.

It is hard to see how any anaesthetist who has a Coxeter-Mushin unit at his disposal could honestly justify the purchase of a new apparatus for use with closed-circuit halothane when for a few shillings his present machine can be satisfactorily and safely modified for this purpose.—We are, etc.,

Ards Hospital, Newtownards, Co. Down. M. A. WOODS. T. A. BROWN.

REFERENCE

1 Brown, T. A., and Woods, M. A., *Brit. J. Anaesth.*, 1958, **30**, 333 and 338.

Sweet Tooth and Decay

SIR,—I was very interested to read in the *Journal* of September 6 (p. 638) Mr. F. T. Ranson's impression that sugar-cane chewing is beneficial to teeth. My practice is in the largest sugar-cane-growing area of this island. It has never been my misfortune to see such a lot of decay in the incisors, and I had been wondering whether the chewing of sugar-cane, in which the incisors would be used much more than in eating other types of softer sweet foods, could have anything to do with it. I have been thinking of doing a small survey and comparing it with a survey in another part of the island where cane is not readily available, but have not got round to it. I would be very interested to know if such a survey has been done elsewhere and with what results.—I am, etc.,

St. Vincent, B.W.I. V. M. USBORNE.

"Flat on Your Back"

SIR,—I have discovered an interesting reaction made by patients during routine examination. On making the request, "Please lie on your back," the patient almost invariably rolls over into the prone position, making it completely impossible to examine the abdomen. In a fairly unselected series, I have found this response in about 80% of patients. It does not seem to depend on the apparent intelligence of the subject. I have noticed that the correct position can invariably be obtained by asking, "Please lie *flat* on your back."

Can anyone explain the psychology of this different response?—I am, etc.,

Birmingham, 29. K. G. BLAND.

Children in Hospital

SIR,—James Robertson (*Journal*, August 2, p. 275), of the Tavistock Clinic, has done a great service by bringing to the notice of the profession the great harm which can result from the admission of the under-4-year-old to hospital. His booklet and film[1,2] are full of stimulating ideas which would be well worth study by all connected with the admission of children to hospital.

I feel that much can be done to make the stay in hospital of the older child a less unpleasant experience. Such simple matters as the time of admission, and the mother being encouraged to give the child its first bath, can make a tremendous difference to the child. I would like to see children allowed to have their own night clothes. These points are brought out in a film I made some years ago.[3] When making that film I found that a child's greatest objection to a stay in hospital was "needle pricks." This led me to work out a premedication avoiding injections. I use "elixir of oblivon" (methylpentynol) in which hyoscine is dissolved. Since my original work I have increased the dose of methylpentynol and now use 1 drachm (3.5 ml.) of the elixir for each stone (6.4 kg.) in weight. The dose of hyoscine varies from gr. 1/150 (0.43 mg.) for children up to 3 years, to gr. 1/100 (0.65 mg.) for children over 4 years old.

These children are induced with a sleep-dose of thiopentone, of which they have no recollection. Another important modification in this technique is the addition of gr. 1/200 to gr. 1/100 (0.33 mg. to 0.65 mg.) of atropine to the thiopentone, as some of the children are not quite "dry" with the hyoscine alone. It is also important to remember that methylpentynol has no analgesic properties, so that some analgesic should be given as soon as the child recovers its vital reflexes. I have used nepenthe for this purpose, but am at present investigating the value of D.F.118 (dihydrocodeine).—I am, etc.,

Worthing. F. R. GUSTERSON.

REFERENCES

1 *Young Children in Hospital*, 1958. Tavistock Publications Ltd., London.
2 "Going to Hospital with Mother." Film, 16 mm. Tavistock Institute of Human Relations.
3 "Premedication and Nursing Care of Children." Film, 16 mm. Central Film Library.

Costs of Notification

SIR,—Last year (*Journal*, May 25, 1957, p. 1241) we wrote to you to draw attention to the remarkable expenditure of money in the notification of infectious diseases. In particular, we mentioned measles as a prime example of a disease whose notification we think to be of no value whatever. We were surprised at how little response our letter evoked. In the past five years 2,162,826 cases of measles have been notified. The cost in notification fees alone for this amounts to over £270,000. Can you, or anyone, tell us to what purpose—other than the provision of pocket money to G.P.s? And what good has come of the notification of acute pneumonia, scarlet fever, or whooping-cough, cases of which total 871,097 at a cost of nearly £110,000?

Enthusiastic G.P.s have in the past five years notified 3½m. cases of infectious disease. It is impossible to assess the cost of the collection, collation, and correction of these figures in terms of paper, postage, and pay-packets, but it can be stated categorically that the notification fees in England and Wales have totalled £406,437. How much longer must this pathetic situation continue?

We do not claim that notification of all infectious disease is useless, and it might be argued that value would arise from the notification of rubella, rheumatic fever, and acute otitis media. We are saddened, however, to think that the £1m. or so that has been uselessly scattered in the past 10 years might have been usefully diverted, for instance, to research in poliomyelitis.—We are, etc.,

Walton-on-Thames. E. O. GIBSON. R. M. EMRYS-ROBERTS.

Why Suffer from Rheumatism?

SIR,—Muscular pain is caused through increases of muscle tension. The physical secondary effects of such increased tension—i.e., mechanical defects and degenerative processes—are the conditions at which the Empire Rheumatism Council has directed its research (*Journal*, October 25, p. 1034). The primary cause of this increased tension in those conditions labelled rheumatism is psychological, and the site affected governed by the mental mechanism of symbolism.

There are complicated relationships between psychic activity and muscular innervations. As long ago as 1892 Freud postulated the conversion of psychic into motor excitement in hysteria. The psychic experiences were unpleasant to discuss, were not apparently remembered, and there was no idea of a causal connexion between exciting cause and the pathological phenomena. The individual suffering from obsessional neurosis is really substituting thought for action. In mild cyclothymics one sees conditions of inhibited and exaggerated phantasy run parallel with variations of liveliness of movement. There appears then to be some reciprocity of muscular innervation with thinking and attention, and an ability for conversion of psychic to motor or motor to psychic energies. To the unconscious mind symbols indicate not resemblance but identity. The child finds the whole world

part of itself; all that he comprehends is part of his own body—a spoon is the same thing as a hand and the door a mouth. Although each individual must create his own symbolism afresh, the association of a common culture and environment precludes great diversities of meaning. Man thinks, feels, and acts symbolically—an economy of effort. What cannot be verbalized can be symbolized; that which causes tension and must not be expressed can be freely shown in a dumb language. Of all organs of the body the musculature is the most freely available for this ambivalent retention and expulsion.

In general practice it can be noticed that interspersed with the patient's complaints of bodily aches and impaired function are varied reactions of tiredness, listlessness, fatigue, sleeplessness, irritability, anxiety, depression, poor appetite, commonly attributed to the physical effects and the limitations imposed on the sufferer. Unfortunately, these psychological reactions receive scant attention; the man has pain, he is unable to work and should be depressed and anxious for his future. It is the taking up of part or all of the symptoms enumerated by the patient that will govern the whole course of the illness and the prognosis. The acceptance of the physical symptoms, with the neglect of the emotional, leads to the use of rubifacients, analgesics, injections, steroids, physiotherapy manipulations, operative measures, and the "157 cures submitted to the research subcommittee of the Empire Research Council." All, on their own, of little more value than simple reassurance and waiting for a spontaneous remission. The taking up of the psychological symptoms, however, leads to the discovery that pains in the knees mean anger and aggression to a child; that lumbo-sacral pain in a young woman expresses a reluctance for intercourse or the fear of pregnancy; that the pain in the arm is a desire to strike out; that the pain in the neck comes because someone is a pain in the neck, and heartache leads to pain in the breast.

Psychotherapy, often the simple ventilation of the problem alone, leads to the relief of muscular tension. Only then will supportive physical treatments help to remove the physical secondary effects of the tension.—I am, etc.,

Sidcup, Kent. L. A. NICHOLS.

Immunization Card

SIR,—I was pleased to see (*Journal*, October 25, p. 1041) that the question of immunization cards has been raised. I think the card provided by Messrs. Glaxo Laboratories Ltd. (*Journal*, October 4, p. 859), which is given to the patient for his or her safe-keeping, would be of more value than having the patient's medical record (E.C.5 and 6) stamped, particularly as the most common cause of confusion is when a patient is taken straight to hospital and is asked about his immunization to tetanus.

Naturally the problem would arise as to the degree of co-operation that could be expected from the public with such a scheme, but if it were made known that this was an important document for the individual's benefit and was regarded with as much significance as the identity card was during the war, I am sure it would be successful. It might even be incorporated within the framework of the medical card.—I am, etc.,

Birmingham, 19. D. H. TARGETT.

"Episol"

SIR,—Your comments on the drug "episol" in "To-day's Drugs" (*Journal*, October 18, p. 974) have an air of irresponsibility arising no doubt from a basis of hypotheses rather than observation. By an extension of your arguments, *para*-aminobenzoic acid should be dangerous, since it contains an aniline structure, though to be just your con-damnation is tinged with the faint praise that allows it possible that this particular benzthiazole derivative may not have a sensitizing potential similar to benzthiazole itself. It does, in fact, remain to be proved that benzthiazole (which is somewhat of a chemical rarity) possesses sensitizing properties; the compound mostly used in the rubber industry is mercaptobenzthiazole.

We have no evidence of any untoward sensitizing potential in episol, but no doubt the occasional idiosyncratic patient will appear during the use of this drug as he does during the use of almost any drug. As far as one is able to assess the clinical properties of the drug, it would appear to entail less risk coupled with a wider scope than well-established compounds containing a benzthiazole structure.—I am, etc.,

J. I. M. JONES,
Director of Research.

Crookes Laboratories Ltd.

**** OUR EXPERT replies: First, I would think that my original note made it quite clear that I was dealing with hypothetical considerations and it is no criticism to tell me that I was. Secondly, a case of benzthiazole sensitivity has been reported.[1] Thirdly, group sensitivity is very common; in such cases one finds that a patient has become sensitive to a whole group of related chemical compounds. Patients who are sensitive to mercaptobenzthiazole are often sensitive to other benzthiazoles. Fourthly, sensitivity to *para*-aminobenzoic acid is indeed well known in group sensitivity with related substances, though Dr. Jones does not seem to realize this. Fifthly, the sensitizing property of an ointment can seldom be realized until the ointment is brought into use; if an ointment for treating fungus infections of the skin sensitizes 1% of the people on whom it is used, it is quite unsuitable. This cannot usually be discovered until it is used on several hundred people. For this reason it is not surprising if Dr. Jones has, as yet, no evidence of a sensitizing potential.

REFERENCE

[1] Bettley, F. R., *Proc. roy. Soc. Med.*, 1952, **45**, 491.

Premonition of Death

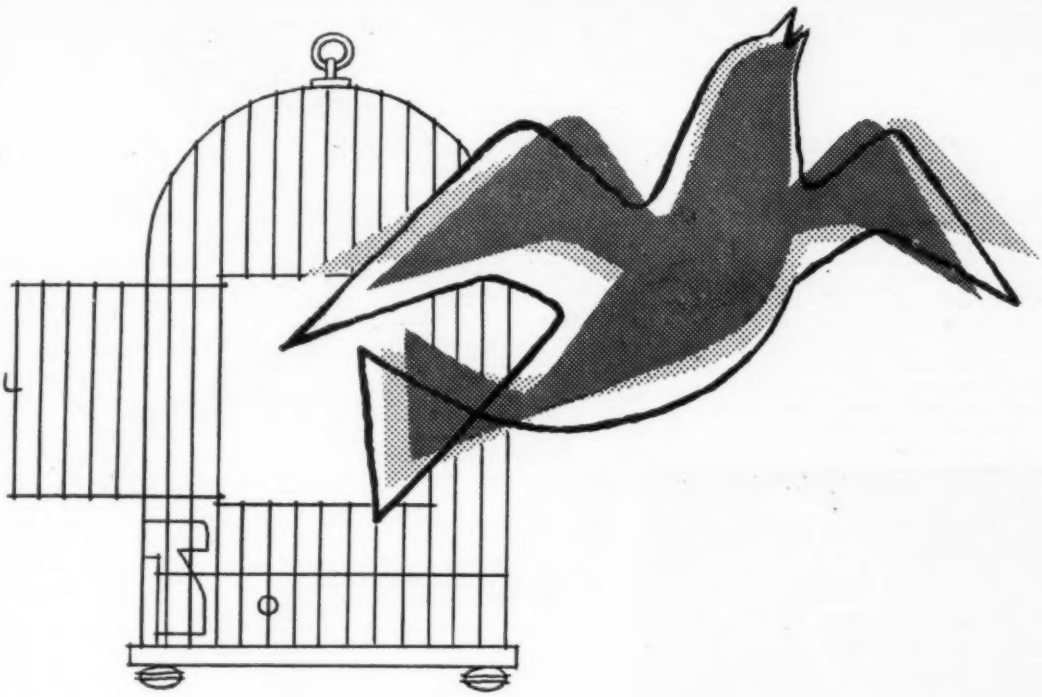
SIR,—While travelling to West Africa in 1941 to serve in a military hospital I was told by an "Old Coaster" that I must expect to see cases of Africans who, having said they were going to die, did so soon afterwards, without any good cause for death being found clinically or at post-mortem examination. Though a good cause of death was found in all instances, a few of my patients told me, soon before the event, that their death was imminent, and I came to associate such an announcement by a patient with a very bad prognosis. I recall one case, however, in which it appeared that psychotherapy, a little crude perhaps, saved the day. The patient was a West African soldier, brought in from the "bush" with pneumococcal pneumonia. He was desperately ill and evidently near death. Very soon after his admission he said to the ward sister, "Sister, I go die"; to which the sister, a Q.A. with strict ideas of discipline, replied, "If you go die, I put you on a charge and you go before commanding officer." The patient's recovery was as rapid as it was unexpected.—I am, etc.,

St. Wulstan's Hospital, Malvern. D. L. H. GODDARD.

Oesophageal Stricture

SIR,—I agree with Mr. K. S. Mullard (*Journal*, November 1, p. 1101) that in the four cases of oesophageal stricture after gastric surgery and naso-gastric intubation that I reported (*Journal*, October 4, p. 817) an unrecognized hiatus hernia was present before the gastric operations were carried out, and certainly some reflux oesophagitis may have been present. But I cannot agree that the appearance of dysphagia in these cases shortly after operation was due to the relief of gastric symptoms by the operations and the unmasking of oesophageal symptoms that had been present before this. In none of my cases had there been any dysphagia before operation, and in one of them barium examination a few weeks earlier had not shown any oesophageal obstruction. Yet in all cases marked dysphagia commenced soon after operation and rapidly increased.

Mr. Mullard surely does not suggest that a reduction after operation in the acid or pepsin content of gastric juice refluxing into the oesophagus and a consequent reduction in oesophagitis can lead to more marked fibrosis and more rapid stricture formation than would have occurred without such a reduction in acid or pepsin secretion. In any case,



Free to breathe again...

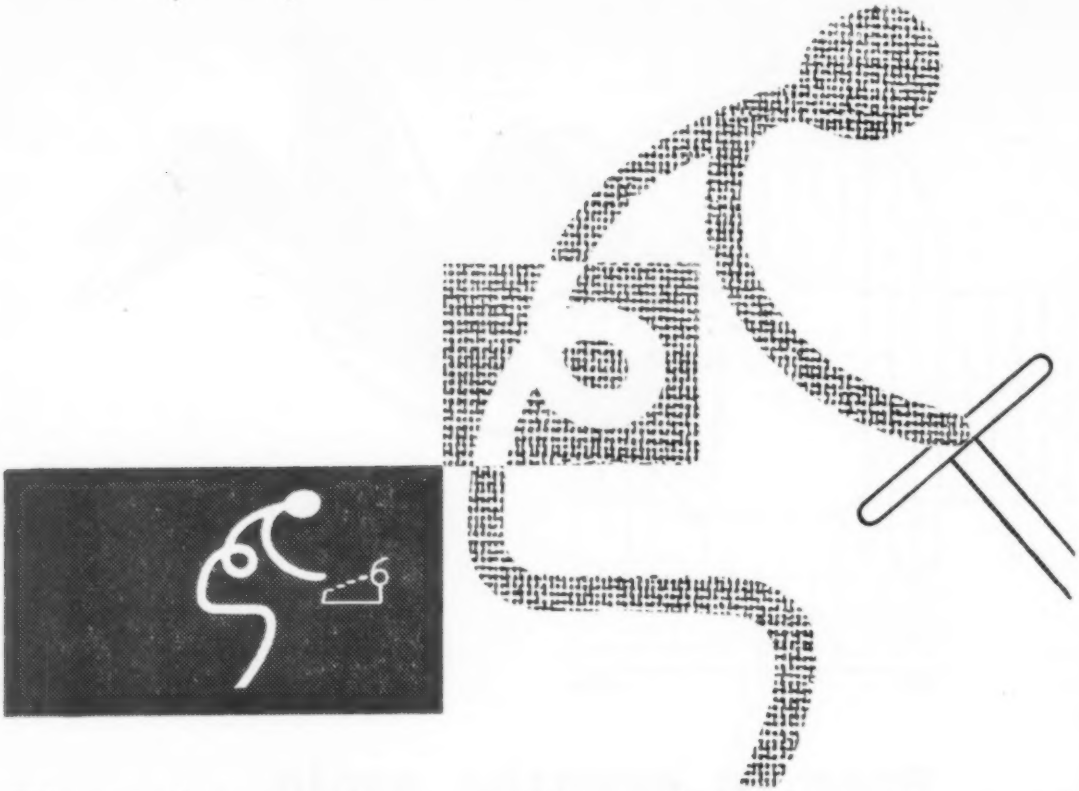
succinctly expresses the relief of the asthmatic subject who uses 'Neo-Epinine' preparations. In the majority of patients 'Neo-Epinine' Compressed Products sublingually or No. 1 Spray Solution by oral inhalation will rapidly relieve the attack. The intractable case will probably require No. 2 Compound Spray Solution, which is more potent and longer acting. 'Neo-Epinine' Compressed Products, 20 mgm., are available in bottles of 25, 100 and 500; 'Neo-Epinine' No. 1 Spray Solution and No. 2 Compound Spray Solution each in bottles of 10 c.c.

'NEO-EPININE' BRAND

ISOPRENALINE SULPHATE

–in bronchial asthma

BURROUGHS WELLCOME & CO. *(The Wellcome Foundation Ltd.)* LONDON



There's a dyspeptic sitting at work right now...

. . . who is making up his mind to come and see you because his usual antacid is failing to give relief. For such patients, Neutradonna, combined with a simple diet, is the treatment to bring the symptoms under control again.

NEUTRADONNA

The Antispasmodic-Antacid

(aluminium sodium silicate and belladonna)

Rapid, sustained symptomatic Relief

In acid dyspepsia and peptic ulcer, prescribe one heaped teaspoonful or three tablets Neutradonna, three or four times a day.

BRITISH SCHERING LIMITED • LONDON

in one of my patients the operation performed was simply closure of a perforation, and this can scarcely have affected acid or pepsin secretion. Moreover, since writing the paper referred to I have seen a similar oesophageal stricture follow an attack of acute pancreatitis. The patient had a laparotomy only, and an indwelling naso-gastric tube was used for several days. Investigation after the onset of dysphagia showed that this patient, too, had a hiatus hernia. It seems clear that if any oesophagitis was present beforehand in these cases it became much more severe in the early post-operative period. I still think the most reasonable explanation is that in these patients, who happened to have hiatus hernias, severe oesophagitis and stricture formation were precipitated by a combination of two factors: (1) the recumbent position adopted post-operatively, and (2) the presence for some days of an indwelling naso-gastric tube.—I am, etc.,

Royal Victoria Hospital, Belfast. J. A. W. BINGHAM.

Resin-rubber Soles

SIR,—Since 90% of children's shoes are now soled with resin rubber, difficulty has arisen in making modifications such as wedging, prolonging the heel, metatarsal bars, and floating out the heel.

I approached a local shoe manufacturer (Messrs. C. and J. Clark, Ltd., Street, Somerset), about this problem, and was shown what a comparatively simple procedure was required—easier to carry out than when dealing with leather-soled shoes—and, provided the correct type of adhesive was used, satisfactory. If managers of orthopaedic workshops carrying out these modifications would like to know the details of the procedure, this manufacturer (and no doubt others) would be prepared to pass on their method and train any orthopaedic workshop operatives in this type of work, free of charge.—I am, etc.,

Bath. HEDLEY HALL.

Dosage of Pancreatin

SIR,—With reference to the letter by Drs. A. D. M. Jackson, A. P. Norman, and W. F. Young (*Journal*, October 25, p. 1039) concerning pancreatin powder for cystic fibrosis, we would like to draw your attention to an additional strength of pancreatin which we have been marketing since 1952 for this condition. The product is "panar granules" (pancreatin) enteric-coated, having a potency of 1½ times pancreatin, *United States National Formulary X*, equivalent to 1½ times pancreatin powder, *B.P. 1958*.—I am, etc.,

Eastbourne. D. PURDIE,
Manager,
Professional Services Department,
The Armour Laboratories.

"On Call to a Nation"

SIR,—In the television programme "On Call to a Nation" (see *Journal*, October 25, p. 1053), in which those taking part were doctors and not actors, I should have thought that the very good-looking general practitioner who spent much time talking to his patients and very little time examining them would have made a better actor than a doctor. When the patient came about his eyes, the doctor pulled down his left lower lid and then told him that he had no disease of his eyes and that all he required was spectacles, and that he should go to an optician for these; he did not have to go to hospital, which was where ophthalmic surgeons worked—they operated on eyes, did cataracts, and so on.

From time to time there have been letters from the general practitioners suggesting that the form O.S.C.1 was unnecessary and a waste of time. If this is the usual method employed by the doctors supplying these forms, I am in entire agreement. I had been interested as we flashed back from time to time to this particular doctor's consulting-room that there was a Snellen chart on his mantelpiece, and I thought at least, when the eye patient came in, that this would be put to a useful purpose, but not a bit of it. I am afraid that this part of the film merely confirmed a complaint of many general practitioners that they were becoming mere agents for directing patients to the suitable hospital department.—I am, etc.,

Camberley. LESLIE HARTLEY.

Congenital Deaf-mutism

SIR,—The dispute between Dr. J. McKenzie (*Journal*, November 1, p. 1102) and his critics as to the site of the abnormality in congenital deafness can be settled only by observation. However, it is pertinent to observe that there is no theoretical reason to suppose that an abnormality of the specialized receptor apparatus of the cochlear duct must be associated with a disorder of the semicircular canals or saccule or utricle. The semicircular canals, for example, appear in their definitive form much earlier than Corti's organ, both in evolution and in development. Any fishmonger's slab will provide evidence that normal semicircular canals can co-exist with a genetically determined failure of development of the cochlear duct. The perennial argument as to whether fish can hear illustrates very well the difficulty of distinguishing vibration from sound in the congenitally deaf.—I am, etc.,

Department of Anatomy, University of Durham. JOHN GRAY.

SIR,—In transcribing my letter on congenital deaf-mutism (*Journal*, November 1, p. 1102) the printer has inadvertently omitted one line of the text in the second sentence. This should read, "I realized only too well the pitfalls associated with this method of examination, but, so far, there is no objective method of proving whether a child is hearing or merely feeling vibration."—I am, etc.,

Department of Anatomy, University of Aberdeen. JOHN MCKENZIE.

Mass Casualties from Nuclear War

SIR,—During the first world war I worked in a C.C.S. at Proven, behind the Passchendaele fighting, in the reception tent. There were three M.O.s working two at a time, 16 hours on, eight hours off. On the first day, so far as my memory goes, we did about 2,000 casualties, and on subsequent days considerably less. The work was essentially sorting the major cases straight to the wards and changing the dressings of the walking wounded. We could do no less, and this work kept us all out, so that after four to five days we were cooked.

I was 33 then and accustomed to the sight of war wounds. We had to deal with disciplined men. We had reliable, experienced orderlies, abundance of stretchers, and I cannot recall being held up for lack of stretcher-bearers. Not all cases by any means were serious; some were literally scratches. This is only a 40-years-old memory, but it is still vivid of physical weariness and the mental horror of just about hating the wounded.—I am, etc.,

King's Langley, Herts. REGINALD FISHER.

SIR,—Your correspondents' views on mass casualties in nuclear war seems to us to be somewhat naive. What, in the name of Hippocrates, leads them to believe that a sufficiency of trained personnel will be left, alive and functioning, to be of any use after an all-out nuclear attack?

What does Colonel T. M. R. Ahern (*Journal*, November 1, p. 1101) propose should be done with the victims of radiation, who must inevitably be a considerable proportion of the casualties still alive? Overdose them with chelates? His statistics seem to us to be reminiscent of the Japanese edict, after Hiroshima, that only the slightly injured should receive any treatment ("3.6 minutes 'doctor's time'"), there being no time and no known treatment for the more seriously injured.

Surely it is incumbent upon the medical profession not to delude itself or allow its prestige to be used in foisting on the public a promise of protection incapable of fulfilment. Civil Defence workers should understand that the very casualties they strive to help may well be dangerously radioactive and thus render these same defence workers themselves casualties. A dustbin lid seems scant shield against a hydrogen bomb. In this nuclear age the old adage "Prevention is better than cure" is our only hope of survival.—We are, etc.,

PAUL Z. HAMMET.
JOANN Z. HAMMET.

Darlaston, Staffs.

Driving Licences

SIR,—Judicious economy is to be welcomed, and the extension of the period of validity of a driving licence from one year to three years will no doubt save both time and labour. Incidentally it will also probably result in some quite unmerited profit to the Exchequer from those who cease to drive owing to death, departure, or disablement.

At times the possession of a long-term driving licence may be a mixed blessing. Thus, a young man who develops occasional attacks of epilepsy, having just acquired a licence permitting him to drive a motor vehicle for the next three years, is under undue temptation to make use of such a licence if he is free from attacks for some months. He may neglect medical advice, but he cannot be accused of having made a false statement for the purpose of obtaining a licence that is valid for three years to come.—I am, etc.,

E. C. O. JEWESBURY.

London, W.1.

After-dinner Speeches

SIR,—Sufferers from the incidence of this complaint (*Journal*, October 11, p. 904) may be interested, even if not particularly heartened, to learn that it does not occur amongst the Chinese. Speeches in that country, whether at official, mercantile, or private functions, are made before the meal, when all are seated at table. The knowledge that those present are far more anxious to eat than to listen, coupled with the shuffling of servants and the clink of dishes and bottles in the background, induces in the host or chairman a desirable brevity, apart from the fact that to keep guests from their food in an unreasonable manner is in itself an act of discourtesy. As a result of this sensible custom dinners tend to be enjoyed by all and not merely by some, while the speeches themselves provide material for leisurely table discussion.—I am, etc.,

H. G. LOWDER.
Commissioner,
Chinese Customs Service (1908-1940).

London, N.W.3.

POINTS FROM LETTERS

Pyrexia Agitans

Dr. H. DE GLANVILLE (Winneba, Ghana) writes: I have just belatedly noticed Dr. A. P. Millar's letter in the *Journal* of June 7 (p. 1355) on this subject, and I recall the instability of my own temperature when recovering in a tropical hospital five years ago from an embolic infective arthritis. My temperature chart refused to settle though I felt well, and showed an unexpected 6 o'clock rise each evening. To avoid this I tried not leaving my bed all afternoon, and not bathing before it was taken, but still the rise occurred. Next day I checked my temperature hourly with the same thermometer, but, although it was subnormal at 5 p.m., it was up again at 6 p.m. The following day I checked it every 10 minutes from 5.30 p.m., and to my considerable surprise it rose suddenly between 5.50 and 6 p.m., and was back to normal or subnormal by 6.20 p.m. I forget the exact figure to which it rose, but it was doubtless something between 99° and 100° F. (37.2-37.8° C.). I persuaded my medical attendant to ignore the chart, and shortly after left hospital and convalesced uneventfully. Since then, however, I have felt certain that in some patients the temperature remains unstable for a prolonged period into convalescence after a febrile illness, and I have been encouraged thereby metaphorically to throw the thermometer out of the window on more than one occasion when it has told a tale at variance with clinical sense.

Obituary

ARTHUR MILLER, F.R.C.S.Ed., D.L.O.

Mr. Arthur Miller, honorary surgeon in charge of the ear, nose, and throat department at both the French and Italian hospitals in London, died in London on October 11. He was 70 years of age.

Arthur Alfonce Miller was born on February 28, 1888, and qualified by taking the London Conjoint diploma in 1916. After qualification he held the appointments of house-surgeon and house-physician at Queen Mary's Hospital for the East End. He then served in France for the remainder of the first world war at various English and French military hospitals. In 1921 he was awarded the Cross of Chevalier of the Legion of Honour for his services to the French sick and wounded. After the war he settled in London as an ear, nose, and throat surgeon. He took the D.L.O. of the English Royal Colleges in 1928, and was elected F.R.C.S.Ed. five years later. He was appointed clinical assistant in his specialty at the Prince of Wales's General Hospital, Tottenham, in 1924, and soon afterwards took up a similar post at the French Hospital. Later he was appointed assistant surgeon to the French Hospital, and in 1934 became full surgeon. For a time in the mid-thirties he was chief clinical assistant at the Central London Ear, Nose, and Throat Hospital, and subsequently became laryngologist to the Italian Hospital. For some years he was also assistant aurist under the London County Council and the Ealing Borough Council, and he had been on the staffs of the British Dental Hospital and the Edgware General Hospital. A member of the Società Italiana di Laringologia, Otologia, e Rinologia, he was a corresponding member of the Société d'Oto-Rhino-Laryngologie of Paris. He leaves a widow.

G. E. P. writes: Arthur Miller worked at the Italian and French hospitals in London for more than 25 years, and in so doing became a household word to these quite considerable colonies of "strangers within our gates." He was known for those two qualities which matter most in medicine—professional skill and the confidence he inspired in his patients. To his colleagues on the staffs of these hospitals I think that he will always be remembered for the brusqueness with which he inadequately concealed the innate kindness of his mind. His loyalty was immutable. In the special work of dealing yearly with patients from no fewer than 20 countries he had those cosmopolitan qualities of mind which it will be hard indeed to replace. His private life was one of simple and total devotion to his wife, and those who were privileged to share happy moments with them in their home life will be with her in heart and sympathy at this time.

H. H. BROOME, C.I.E., M.B., Ch.B., F.R.C.S.

Lieutenant-Colonel H. H. Broome, a former principal of King Edward Medical College, Lahore, died at Salisbury on October 31. He was 83 years of age.

Harold Holkar Broome was born on March 6, 1875. From Owens College, Manchester, he went on to Edinburgh University as a medical student, and graduated M.B., Ch.B. in 1898. Distinguishing himself greatly as a student, he won several prizes and scholarships and a medal in practical anatomy. Returning to Owens College, he was junior demonstrator in anatomy, and after a term as house-surgeon at the North Lonsdale Hospital, Barrow-in-Furness, he returned to the college to become senior demonstrator in anatomy. He took the London Conjoint diploma in 1901, and was admitted F.R.C.S. in 1913. In 1903 he was awarded the Martin Memorial gold medal and entered the Indian Medical Service as a lieutenant. Five years later he was appointed professor of anatomy at the King Edward Medical College, Lahore. During the first world war he served on the North-West Frontier of India and in Meso-

potamia and German East Africa. Returning to India after the war, he was professor of surgery at King Edward Medical College from 1922 to 1930, and for most of that time was its principal. While holding these posts he was appointed C.I.E. in the New Year Honours List of 1929. A Fellow of Punjab University, he had been dean of its faculty of medicine. He retired from the I.M.S. in 1930. A member of the British Medical Association for over fifty years, he was president of the Punjab Branch in 1929–30. During the second world war he came out of retirement to act as medical superintendent and surgeon at the Alverstoke Emergency Hospital at Gosport, Hampshire. In 1902 he married Miss Clara Alice Finney, by whom he had two sons.

ALEXANDER MELLICK, M.D., F.R.F.P.S., D.O.M.S.

Dr. Alexander Mellick died suddenly at his home in Glasgow on October 19 at the age of 55. Though he had been under medical care for some time he had attended the meeting of the Orthoptic Society in London the previous day.

Alexander Mellick was born in Glasgow on July 23, 1903, and attended Alan Glen's School and Glasgow University, where he graduated in science in 1924, and medicine in 1926, proceeding to the M.D. five years later. He started his professional life as a general practitioner in the East End of Glasgow, with an attachment as physician to the out-patient department of the Glasgow Royal Infirmary. In 1933 he seized an opportunity to join the staff of the Glasgow Eye Infirmary as a clinical assistant. Becoming surgeon in charge of wards in 1949, he was admitted a Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow in that same year. A man of quiet and retiring disposition, he was widely read in both medicine and ophthalmology. This medical bent was shown in his ophthalmological practice, and found scope in his appointment as consulting ophthalmic surgeon to the Southern General Hospital, Glasgow, and to the infectious diseases hospitals. He had done original work in orthoptics, and in the last few years he was surgeon in charge of the Orthoptic School at the Glasgow Eye Infirmary. He also became a member of the Orthoptic Board. Dr. Mellick was very musical, and a brilliant pianist. His death is a loss to ophthalmology, and in particular to orthoptics in Glasgow. He leaves a widow.

J. G. MacKENNA, M.B., Ch.B., D.P.H.

Dr. J. G. MacKenna, honorary consulting physician to the Royal Alexandra Infirmary, Paisley, died at his home at Paisley on October 16. He was 80 years of age.

John George MacKenna was born at Dumfries on March 20, 1878, the son of the Rev. Robert MacKenna. He was educated at Dumfries Academy and at the Royal High School, Edinburgh. He then entered Edinburgh University as a medical student, graduating M.B., Ch.B. in 1900. After graduation he held the appointment of assistant surgeon at the Southern Dispensary, Liverpool, for six months, returning to Edinburgh to take the D.P.H. of the Scottish Royal Colleges in 1901. In the same year he was appointed assistant medical officer of health and assistant bacteriologist at the Paisley Infectious Diseases Hospital. In 1907 he settled in private practice in the town, and, later, was appointed assistant surgeon to the Royal Victoria Eye Infirmary. For over thirty years he served the Royal Alexandra Infirmary, first as assistant visiting physician and then as full physician, and when he retired in 1944 he was appointed honorary consulting physician. Dr. MacKenna had many interests outside his profession. A staunch Liberal, he became president of the Paisley Liberal Association. On one occasion, when he took the chair at a political meeting at which both Mr. Herbert Asquith and Mr. David Lloyd George were among the speakers to a packed audience, he conducted the proceedings so successfully that Mr. Asquith afterwards described him as the finest chairman he had ever sat under.

J. S. D. writes from Paisley: As a contemporary of the late Dr. John MacKenna I cannot help feeling that his death has cast a gloom over this town and the medical profession, of which he was a worthy and highly respected member for many years. Starting at the beginning of the century, he built up a large practice, and to his patients he was guide, philosopher, and friend in their illnesses and worries. Interested in literature, he read much and was an excellent public and after-dinner speaker. His chief sport was cricket, which he played in his early days, and in which he took a great interest till the end. Of a quiet, courteous nature, and endowed with a cultured mind and sound judgment, he attracted many friends, who enjoyed his company and conversation. Reared in the manse, he had strong religious convictions, which he consistently practised throughout his life. Retiring from practice several years ago owing to ill-health, which fortunately did not completely incapacitate him, he continued to take an alert interest in all around him till the end, which came, as he had wanted it, very quickly. To his widow, son, and daughter we extend our sincere sympathy.

KATHERINE J. S. CLARK, M.D., D.P.H.

Dr. Katherine J. S. Clark, for many years a school medical officer in Edinburgh, died at her home there on October 6. She was 92 years of age.

Katherine Jane Stark Clark, the fourth of the nine children of the Rev. John Clark, a minister of the United Presbyterian Church at Hardgate, Kirkcudbrightshire, was born on July 15, 1886. The whole family of nine went to Edinburgh for their education, and Katherine Clark attended the Merchant Company's School which is known as the Mary Erskine School. After leaving there she trained as a nurse at Dundee Royal Infirmary, and then spent some years doing private nursing. At this time she took an active part in the campaign for women's suffrage and in the efforts to gain advanced university education for women. When the University of Edinburgh decided to admit women to the professional examinations she made up her mind to enter the extra-mural school of medicine for women. She graduated M.B., Ch.B. in 1903, and then served as a house-physician at Leith Hospital and as resident medical officer at Craigleith (now the Western General Hospital). In 1906 she obtained the D.P.H. of the Scottish Royal Colleges. In the following year she proceeded to the M.D., taking rheumatism in children—in which she was very interested—as the subject for her thesis. For some time she was a school medical officer in Yorkshire, but in 1910 she returned to Edinburgh to take up a similar appointment under the School Board, and continued to work in the schools until her retirement in 1931. During the first world war she joined the R.A.M.C., and, when the Queen Mary's Army Auxiliary Corps was organized, was appointed medical controller in the Scottish Command, attaining the rank of colonel. At that time some doubt was expressed whether she was a member of the R.A.M.C. or of the Women's Army, but it was decided that she was in the R.A.M.C. After retirement she continued to lead a full and active life. A pioneer in her own work, she maintained her interest in the immense progress made in the care of children under local authorities. She was associated with many professional and social service organizations and gave outstanding service to the community. She found relaxation in the management of her home, in gardening, and in travel, and was happy with her books and her friends almost to the end. She died after a short illness, leaving many friends of a younger generation to remember her with pride and affection.—J. K. R.

C. W. JENNER, L.M.S.S.A.

Dr. C. W. Jenner, who had been living in retirement at Manningford Bohune, Wiltshire, died on October 22 at the General Infirmary, Salisbury. He was 74 and had formerly been in practice in Haslemere, Surrey.

Cyril William Jenner was born at Durrington, Wiltshire, on September 16, 1884. His forebears were well known in Wiltshire for over 200 years, and he was a great grand-nephew of the celebrated Edward Jenner, the pioneer of vaccination. After going to school in Cirencester and Salisbury he became a medical student at the London Hospital and qualified in 1913. Soon afterwards he went into practice in Haslemere, where he remained, an esteemed family doctor, for 44 years. On his retirement he had served the Haslemere Hospital for 43 years, being for many years chairman of the medical staff committee and a member of the house committee. He was keenly interested in all aspects of the hospital life, and, with the able assistance of his wife, was largely responsible for the acquisition and equipping of St. George's ward as a maternity unit. He also served on the medical advisory committee of the Guildford group of hospitals, and his quiet confidence and wise counsel were appreciated by all.

During the 1914–18 war he served as a captain in the R.A.M.C. in Gallipoli, Egypt, and Palestine, being attached to the 2nd South Midland Mounted Brigade Field Ambulance. A lover of Gilbert and Sullivan, he was a member of the cast in many productions at Haslemere during the period between the wars. For many years he rarely missed a meeting of the Guildford Division of the British Medical Association, being chairman of the Division in 1949 and one of the representatives at the Annual Meeting of the Association in Dublin in 1952. He did not consider that there was sufficient reason to alter course and give evidence before the Royal Commission, but once a firm decision had been reached he was prepared to co-operate. Only last year he resigned from the Surrey Local Medical Committee: he had been a member of it and of its predecessor, the Surrey Insurance Committee, for 35 years, a magnificent record of voluntary service.

The very large congregation at the memorial service on a recent Saturday afternoon in Haslemere Church was the fitting tribute of friends, patients, colleagues, and nurses to his long years of untiring and devoted service.—C. P. W.

IVOR CHANCE, M.B., B.S.

Dr. Ivor Chance, who had only recently established himself in general practice at Reading, died at Middlesex Hospital on October 27, four days before his 35th birthday.

Ivor Chance was born on October 31, 1923, the son of the late Major Maurice Chance, of Dorking. Receiving his medical training at the Middlesex Hospital, he graduated M.B., B.S. in 1948, and then held the appointments of house-surgeon in the ophthalmic department at Middlesex Hospital and house-physician in the cardiology department at Ashford Hospital, Middlesex. From 1955 until earlier this year he worked at a mission hospital in Uganda. He leaves a widow and two sons and two daughters.

W. R. B. writes: In 1955 Ivor Chance decided to give up his plans for obtaining a practice in England in order to work for three years in a mission hospital in Uganda. While at Mengo Hospital, Kampala, he threw himself with characteristic energy into all the varied activities of medical missionary work. Paediatrics was his great interest, and he spent much time devising plans for the new children's ward, in which the mothers are given their own dormitory and courtyard. To deal with the problem of kwashiorkor he enlisted the help of Church World Service of America, and in co-operation with the Y.W.C.A. arranged for many tons of dried milk powder to be distributed to the under-5-year-olds in central Uganda. He did a great deal to help the Sanyu Home for motherless babies in Kampala, working hard to improve the facilities and the diets for these children. At the time of his death he was enlisting fresh support in England for the home, and had plans for an extension of cottage homes and foster-parents for the many orphan children in Uganda. In 1958 he returned to England for family reasons, and had just begun in practice in Reading when overtaken by his final illness. Although he was in Uganda for only three years, he made a lasting impression not only by his professional keenness but by his warm-hearted friendliness and generosity, his transparent sincerity, and his true Christian witness. He is remembered with gratitude and affection by many hundreds of his friends of all races, who think of him as a real friend and brother as well as a beloved doctor.

D. C. DRUITT, M.R.C.S., L.R.C.P.

Dr. D. C. Druitt, who was in general practice at Petworth, Sussex, for some 40 years, died there on October 12. He was 73 years of age.

Daniel Cuthbert Druitt was born at Christchurch, Hampshire, on August 12, 1885. His father was a solicitor, but his grandfather and great-grandfather were doctors. His grandfather, Dr. Robert Druitt, who died in 1883, was the author of the well-known *Surgeon's Vade Mecum*, which passed through eleven editions, and of a small work entitled *Cheap Wines, Their Use in Diet and Medicine*; he also had the distinction of being one of the last to receive the Lambeth M.D., which was granted to him in 1878. From Felsted School Daniel Druitt went on to Guy's Hospital for his medical training, and qualified M.R.C.S., L.R.C.P. in 1909 and then entered general practice at Saffron Walden, Essex. He served in the R.A.M.C. in the first world war from 1916 onwards, and was appointed to the Order of Leopold. In 1919, soon after his return to civilian life, he settled in general practice at Petworth, where he became also honorary surgeon to the cottage hospital.

A colleague writes: Dan Druitt came into general practice at Petworth in 1919, and in the subsequent forty years accepted the challenges of country practice and adapted himself to the tremendous changes which occurred during that time. He was a good doctor, a first-class diagnostician, and always maintained that he knew a little about everything and not too much about anything. In 1952 he retired from full-time practice because of illness, but continued to take an active interest in many of his patients. He was a family doctor, a lovable and kind man.

D. B. McGRIGOR, O.B.E., M.B., Ch.B., D.M.R.E.

D. C. B. writes: May I add a small personal note about Brigadier D. B. McGrigor, whose obituary you recently published (November 1, p. 1108)? I worked with him in Millbank in the 'twenties, and I had the privilege of his friendship ever since. He was a fine man, tall and handsome—he never lost his erect carriage even in the later years of his life—warm and generous. I never saw him during the last war, but afterwards it was a pleasure, and illuminating, to listen while he told of men and events during the war, for, whilst he was kindly in his judgments, he had a keen eye for frailties. "Elegant" was a favourite word of his, and he used it to describe a man who might, but need not, be eminent in his profession, but who was a man of whom men could approve. In this sense he was indeed an "elegant" man, and he will be missed by a very wide circle of friends all over the world.

afe, selective sedation and muscle relaxation
otent, well-tolerated oral oestrogen replacement

rade mark

ttles of 20 and 100 tablets (each of 200 mg. meprobamate
.01 mg. ethinyloestradiol).

Ed.2

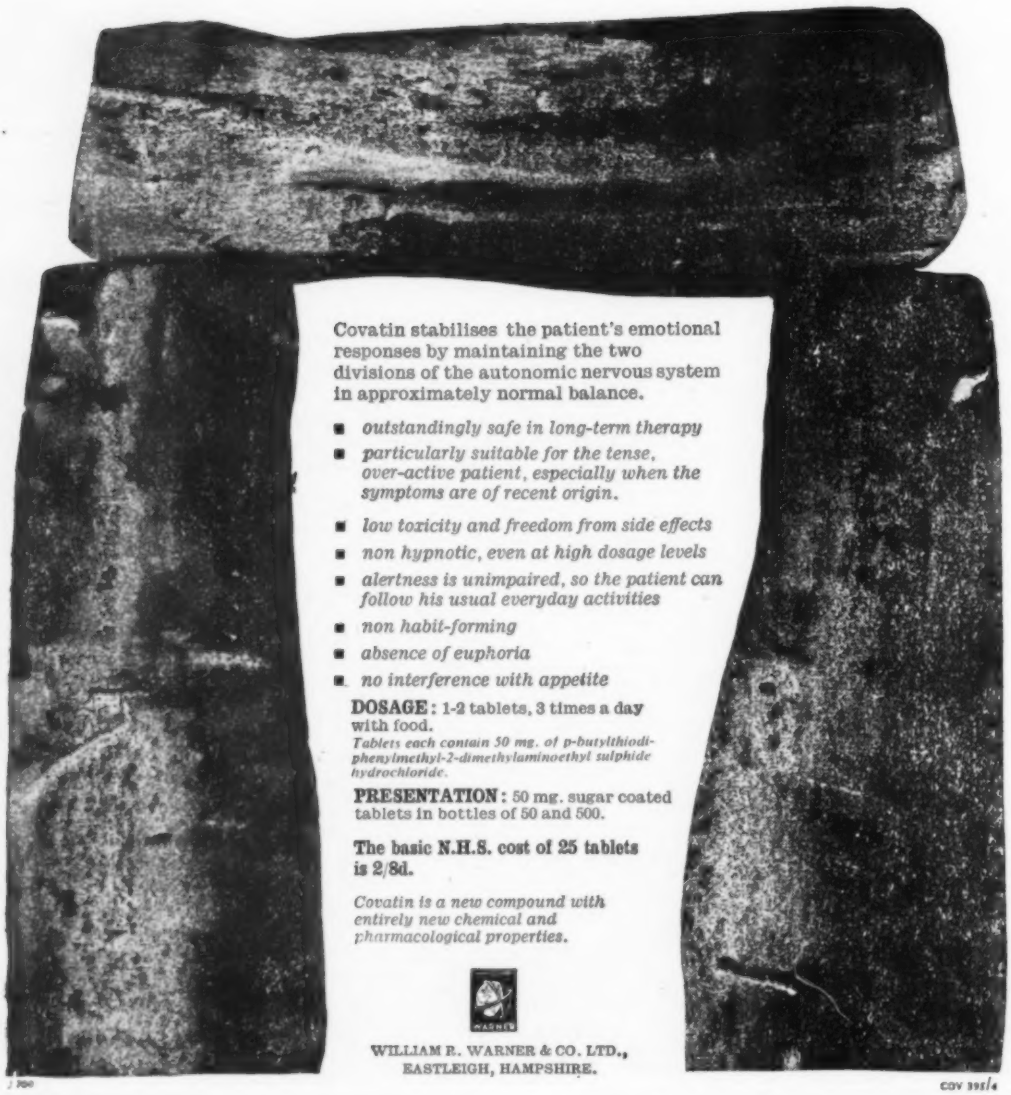
Equadiol

John Wyeth & Brother Limited, Clifton House, Euston Road, London, N.W.

COVATIN

(Captodiame) TRADE MARK

safely restores emotional stability



Covatin stabilises the patient's emotional responses by maintaining the two divisions of the autonomic nervous system in approximately normal balance.

- *outstandingly safe in long-term therapy*
- *particularly suitable for the tense, over-active patient, especially when the symptoms are of recent origin.*
- *low toxicity and freedom from side effects*
- *non hypnotic, even at high dosage levels*
- *alertness is unimpaired, so the patient can follow his usual everyday activities*
- *non habit-forming*
- *absence of euphoria*
- *no interference with appetite*

DOSAGE: 1-2 tablets, 3 times a day with food.
Tablets each contain 50 mg. of p-butylthiodiphenylmethyl-2-dimethylaminoethyl sulphide hydrochloride.

PRESENTATION: 50 mg. sugar coated tablets in bottles of 50 and 500.

The basic N.H.S. cost of 25 tablets is 2/8d.

Covatin is a new compound with entirely new chemical and pharmacological properties.

WARNER

WILLIAM R. WARNER & CO. LTD.,
EASTLEIGH, HAMPSHIRE.

COV 391/4

Medical Notes in Parliament

HOUSE OF LORDS

Alcohol and Road Accidents

On November 4 Lord AMMON asked if the Government could now announce the publication date of the report from the Medical Research Council on the relation of drink and road accidents. Lord HAILSHAM, Lord President of the Council, replied that a paper giving the results of the experimental work conducted under the auspices of the Medical Research Council on the effect of alcohol upon the skill of drivers of motor vehicles had already been published in the *British Medical Journal* on October 25, 1958.* A more detailed presentation of the methods used, and the data upon which the conclusions were based, would be published by the M.R.C. in due course.

Report in "British Medical Journal"

Lord AMMON asked for the reason for the continual delay in publishing the report. "Is it usual to publish a report to this House in a journal before Parliament receives it?"

Lord HAILSHAM.—My Lords, with regard to the first part of the question, the reason for the delay in the publication of the full report is that those concerned have not yet completed the draft. The answer to the second part of the question is that it was thought desirable to give the findings to the public as soon as possible. When the full report came he understood that it would add nothing of importance, so far as the general public were concerned. It would, however, be of interest to other research workers in that it would give full experimental details. Lord AMMON asked if the Lord President did not know that an extract from the report was published in the *British Medical Journal* and an indication that they had the full report, and, in fact, had had it for some time? Lord HAILSHAM said the *British Medical Journal* did not have the full report because it was not ready. What was published on October 25 was a paper giving the results of the experimental work.

Lord MATHERS asked the Lord President whether he was aware that on several occasions publication of the report had been promised by the Government? What purpose was intended to be served by withholding the report from publication?

Lord HAILSHAM said the Government was not withholding publication of the report. They would publish it as soon as they had it. What was holding up its publication was the fact that the author or principal draftsman of it, as a university professor of psychology, was an independent worker who had undertaken this work with the aid of a grant from the Medical Research Council. He had been asked to produce the report as soon as possible, but there must be some limit to the amount of pressure put on a person in that position. There was no question of the Government's not making up its mind. It was a scientific report, and it was not ready yet.

QUESTIONS IN THE COMMONS

Atomic Radiation Effects

The PRIME MINISTER was questioned on November 4 about the United Nations Scientific Committee's Report on the dangers of radiation. He said he had given careful study to the report, and also to the statement on the report by the Medical Research Council presented to Parliament last August. In their consideration of all questions relating to the effects of radiation the Government would take the conclusions of the report into account. Mr. J. RANKIN (Glasgow, Govan, Lab.) asked him if he was now prepared to say that it was the Government's view that nuclear tests should be stopped for ever. Mr. MACMILLAN replied that the report made clear that the radiation dose to be expected from the fall-out of tests was minute compared with other causes, both natural and man-made. Some of these natural causes were due to the geological formation and radioactivity of rocks, and so forth, which were matters for further study. The man-made causes included luminous watches, clocks, television receivers, and shoe-fitting fluoroscopes. Regarding the latter, action had been taken by the Home Secretary. A committee under the chairmanship of Lord Adrian was inquiring into diagnostic radiology, and that was perhaps one of the most important aspects of it. There was also the question of occupational exposure among some industrial, medical, and atomic-energy research workers. There careful and minute medical procedure was carried out, but if it was necessary to tighten up that procedure they would examine that too.

Mr. PHILIP NOEL-BAKER (Derby, South, Lab.) called attention to the statement the previous week of the chairman of the U.S. Atomic Energy Commission that the U.S. made 32 test explosions last year, not 16 as had been previously declared. Did that mean that the studies made by the United Nations Committee and the M.R.C. were based on incomplete information about the amount of radiation released by tests? Mr. MACMILLAN said, "No." But apart from the radiation side there were other aspects. From natural and other man-made causes there were far greater dangers than from tests. "Of course, I hope we shall reach agreement on abolishing the tests, but I think the matter should be held in proportion."

Radio "Scatter" Stations

Mr. CHARLES ORR-EWING, Under-Secretary of State for Air, answered several questions on November 5 about the high-power tropospheric forward-scatter stations to be constructed in this country for N.A.T.O., and the possible effects of radiation from them on people living in the locality. He stated that the plans were still being examined. The stations were for radio communication, and not radar warning. Local authorities would be consulted whenever this was required. The stations would be so designed and located that no radiation hazards would arise to the general public, nor would any houses have to be evacuated. He was asked what was the scientific basis for this statement, and replied that the conclusion had been reached after mature consideration and consultation with the Medical Research Council, which was satisfied that radiation at the relevant wavelength had a thermal effect only, and that there was no biological effect.

Subliminal Advertising

Mr. NESS EDWARDS (Caerphilly, Lab.) asked the Postmaster-General to what extent he had been consulted under Section 4(5) of the Television Act, 1954, about the use of subliminal advertising by the Television for South Wales and the West of England contractors, and how far this form of advertising conformed to his approved rules. Mr. ERNEST MARPLES said that subliminal advertising would be contrary to the first paragraph to the Second Schedule of the Television Act. There had been no reason, therefore, for consultation or direction under Section 4(5) in this respect. The Authority had been assured by Television for South Wales and the West of England that the "keep watching" sign was transmitted at speeds at which it could be plainly seen, and that in any case the use of the message had ceased on October 21. The Authority also informed him that subliminal transmissions in any form were prohibited in its programmes, with the possible exception of some scientific programmes in which subliminal techniques would be openly examined.

On November 6 Mr. J. STONEHOUSE (Wednesbury, Lab.) asked the President of the Board of Trade whether he was aware of the dangers of the use of subliminal techniques

*See Drew, G. C., Colquhoun, W. P., and Long, H. A., *Brit. med. J.*, 1958, **2**, 993.

for advertising and other purposes; and if he would take steps to ban their use. Sir DAVID ECCLES said he understood that these techniques could be used in cinemas and on the television. Their use in cinemas would be subject to the local licensing authority.

Mr. STONEHOUSE: Is the right hon. gentleman aware of the very welcome lead given by the Institute of Practitioners in Advertising, which has declared these sinister techniques professionally unacceptable? Would he follow that lead and ban these techniques from all kinds of communication? Further to that, could he say what was being done about the importation of American horror films which use these techniques? Sir DAVID ECCLES said it was really not the Board of Trade's responsibility to ban these techniques from all forms of communication. He thought his responsibility rested probably on the part of the supplementary question which referred to the import of films. If they contained these practices and they were found to be bad, the Government would certainly see what could be done about it.

Law on Attempted Suicide

Mr. KENNETH ROBINSON (St. Pancras North, Lab.) asked the Home Secretary what progress he had made in his consideration of the law relating to attempted suicide. Mr. R. A. BUTLER told him that before a change in the law was proposed it was necessary to ensure that persons who attempted suicide, and needed care but could not be given it, or would not accept it, unless they were brought before the courts, could be looked after by other means. He was still studying this difficult problem, and could not at this stage give an undertaking about when legislation could be introduced.

Scottish Lunacy Law

Dr. J. DICKSON MABON (Greenock, Lab.) asked the Secretary of State for Scotland on November 4 if his consultations with the professional and other organizations concerning the Russell Report on Scottish Lunacy were concluded; and what action he intended to take. Mr. J. S. MACLAY replied that, at his request, the Scottish Health Services Council were considering the application to Scotland of the recommendations of the Royal Commission on Mental Health in England and Wales in the light of the Scottish White Paper issued in 1955. He had received their first report. He had also other memoranda from interested bodies under consideration. He expected to receive a second and final report from the council early next year.

Cyprus Doctors' Suggestion

Mr. D. WADE (Huddersfield, L.) asked the Secretary of State for the Colonies what answer had been given to the proposal by the Human Rights Committee of the Cyprus Medical Association that one of its members should be present at the post-mortem examination of persons who died while in the hands of the security forces in Cyprus. Mr. J. PROFUMO, Under-Secretary, stated that the Governor was considering the representations made to him on October 23. Mr. WADE, while recognizing the extreme provocation with which the troops were faced, asked if it would not be wise to take any opportunity to provide evidence to the people of Cyprus and the world that no unnecessary violence was used by the security forces, in spite of that provocation. Mr. PROFUMO said the Governor would have all these matters in mind when he considered the representations.

Polio Vaccine

Mr. FENNER BROCKWAY (Eton and Slough, Lab.) asked why supplies of the anti-poliomyelitis vaccine produced by the Glaxo Laboratories at Stoke Poges were not distributed after April; and for what period this hold-up continued. Mr. WALKER-SMITH said he understood that production difficulties intervened. He could not yet say when the distribution of vaccine from this manufacturer would be resumed.

Royal Commission on Doctors' Pay

Mrs. LENA JEGER (Holborn and St. Pancras, South, Lab.) asked the Minister of Health on November 10 when he expected to receive the report of the Royal Commission on doctors' pay. Mr. D. WALKER-SMITH.—The Commission are still taking evidence and collecting necessary information. They expect to be able to submit their report about next summer.

Composition of Flour

Mr. M. LIPTON (Brixton, Lab.) asked the Minister of Agriculture, Fisheries, and Food when the Food Standards Committee would complete their report on the composition of flour and bread, which had been under consideration since May, 1956. Mr. J. B. GODBER, Parliamentary Secretary, said that an interim report dealing with milk bread would be available early in the new year. The Minister understood, however, that investigation of the technical problems involved was taking longer than the committee had expected and that it would be some little time before the drafting of their main report could be put in hand.

Chronic Disease.—At the end of 1957 nearly 10,700 names were on waiting-lists for 57,600 chronic sick and geriatric beds in Health Service hospitals in England and Wales (Minister of Health, November 10).

Medico-Legal

THE CHEMISTS' FEDERATION JUDGMENT

[FROM OUR LEGAL CORRESPONDENT]

Judgment was given on November 3 by the Restrictive Practices Court in the Chemists' Federation case (*Journal*, October 18, p. 985, and October 25, p. 1049). The reserved judgment giving the Court's reasons for its general conclusions expressed on October 13 was delivered by Mr. Justice Devlin (*The Times*, November 4).

He started by explaining the principle adopted by the Federation that proprietary medicines should only be sold to the public by or through registered pharmacists. The restriction which the Court had to consider sought to control all medicines in the same way as the sale of medicines containing poisons or other dangerous substances was controlled by the Pharmacy and Poisons Act, 1933. The machinery through which control was exercised was the C.F. List, which originated in the desire of retail chemists to protect themselves from what they regarded as unfair competition. Manufacturing members of the Federation agreed that all their products falling within the definition "medical preparations" might be put on the List and distributed only to wholesalers who were members of the Federation. These undertook to supply them to retail chemists only. Sale was not restricted to retail chemists who were members of the Federation, nor were the retailers required to sell C.F. List goods only, although they were expected to promote the sale of C.F. goods as against non-C.F. goods.

Court's Task

By Section 20 (1) of the Restrictive Trade Practices Act, 1956, the Court was required to consider whether this restrictive machinery was contrary to the public interest. They were not to answer this question as a matter of policy, but by the test formulated by Parliament in Section 21 of the Act, which provided that a restriction was contrary to

Case History of Mr. Polly

"Mr. Polly was sitting on a stile . . . and suffering acutely from indigestion. He suffered from indigestion now nearly every afternoon in his life . . . Wonderful things must have been going on inside Mr. Polly. It must have been like a badly managed industrial city during a period of depression; agitators, acts of violence, strikes, the forces of law and order doing their best, rushings to and fro, upheavals . . . the rumbie and thunder of the tumbrils . . ."

From "The History of Mr. Polly", by H. G. Wells (by permission)

In a later day the forces of law and order would have been reinforced by Belladenal Retard —and peace restored.

Belladenal Retard

BY **SANDOZ**

antispasmodic, anticholinergic, central sedative

TABLETS:
0.25 mg. total alkaloids of belladonna
50 mg. Phenobarbitone B.P.

Sandoz Products Limited

Sandoz House
23 Great Castle Street
London, W.1

The Climacteric . . .

". . . . a mixture of the male and female hormones was more efficacious than œstrogen alone." Brit. Med. Journ. 1953 (*July* 25), 2.214

The association of methyltestosterone and ethinylœstradiol in Mepilin produces a more complete response in the treatment of menopausal disorders than can be obtained by the use of œstrogens alone. An increased feeling of confidence and well-being is produced which is both mental and physical.

The presence of methyltestosterone enables a reduction in œstrogen dosage to be made; thus undesirable side effects such as breast turgidity and pelvic congestion are avoided and the risk of withdrawal bleeding is reduced.

MEPILIN TRADE MARK ELIXIR & TABLETS

Each teaspoonful (4 ml.) of Mepilin Elixir and each Mepilin Tablet contains ethinylœstradiol 0.01 mg. and methyltestosterone 3 mg.

'MEPILIN' TABLETS. Bottle of 25 at 4/- and 100 at 12/-
'MEPILIN' ELIXIR. Bottle of 4 fl. oz. at 6/- and 500 ml. at 20/6 Basic N.H.S. prices

Dosage: Menopause and geriatric conditions: average cases — 3 tablets or 3 teaspoonfuls daily.

THE BRITISH DRUG HOUSES LTD. (MEDICAL DEPARTMENT) LONDON N.1 BDH

Treatment of **ASTHMA** *with*

NORADRAN INHALANT

ADVANTAGES

★ UNIQUE FORMULATION ★ HIGH SAFETY MARGIN
★ RAPID & POWERFUL THERAPEUTIC EFFECT ★ ABSENCE OF DRYNESS & TIGHTNESS OF RESPIRATORY TRACT.

NORADRAN INHALER—*Unique construction and performance—all glass—designed for efficiency and compactness : issued in polythene box suitable for pocket or handbag.*

NORADRAN INHALANT
FORMULA :
Isoprenaline Sulphate B.P.—1%.
Dihydroxypropyl-7-Theophylline—5%.
Papaverine Hydrochloride B.P.—0.99%.
in special aqueous solvent.
PACKING : 15 c.c. bottle.

NORMA CHEMICALS LTD.
198 FINCHLEY ROAD, LONDON, N.W.3

public policy unless it fell within one of the seven categories set out in the section and was not unreasonable having regard to the balance between the relevant circumstances and any detriment to the public resulting from the restriction. The Court's task was that of any ordinary court of law, to construe the words of the Act and to see if upon the facts proved the case fell within them.

Protection of Only a Small Minority

The Federation's case was that their restriction fell within category (*a*) or (*b*) of Section 21. The case under category (*a*) was that the restriction was reasonably necessary to protect the public against injury in connexion with the consumption and use of medicines. The only significant difference between the sale of medicines by an unqualified person and by a chemist was that, if the chemist was told by the customer of the condition to be relieved, he had the training and ability to select the appropriate remedy. The C.F. restriction did not, however, require C.F. List products to be sold only by the chemist himself and not by his unqualified assistants. The restriction would protect only a small minority who, while in doubt about the right medicine to buy, had not the sense to ask for advice from a qualified person but yet gave some manifestation which would cause the chemist to make some inquiry about their condition. On the evidence the risk of injury through buying from unqualified persons could not be rated so high as to say that it balanced the detriment to the public from not being able to buy commodities it wanted from any retailer who was willing to sell them.

The Federation's case under category (*b*) was that the removal of the restriction would deny to the public specific benefits. These were: the opportunity which it afforded chemists to give advice; the work of the Federation's standards committee, which examined the formulae of medicines on the List for suitability and examined claims relating to their performance to see whether they were justified; and that it was only the protection from competition afforded by the restriction which kept country chemists in business and so available for the National Health Service.

The Court was not satisfied by the evidence on any of these heads that the restriction was justifiable under Section 21.

No Immediate Injunction

The Registrar had applied under Section 20 (3) for an injunction. The Court did not think that Parliament had intended any approach other than the normal rule that an injunction, breach of which carried committal as a penalty, would be granted only if there was reasonable apprehension that an offence was about to be committed or repeated. Until the judgment the Federation had not known whether its restriction would be declared illegal under the new Act or not. The Federation would be given a reasonable time to put its affairs in order, and should not have to do so under the shadow of an injunction. If the Registrar was dissatisfied with what was done he could apply to the Court specifying the particular activities he desired to be restrained.

The order of the Court would therefore consist simply of a declaration in the terms specified in the judgment.

DEAF-AND-DUMB DRIVER FINED

[FROM OUR LEGAL CORRESPONDENT]

On September 29 a deaf-and-dumb driver, Arthur James Callaway, aged 49, was fined £5 at Worthing for careless driving (*Daily Telegraph*, September 30).

When the chairman of the justices expressed surprise that Callaway, who communicated with the court through a deaf-and-dumb-club interpreter, should have been able to pass his driving test, particularly as he could not write and even had difficulty in interpreting deaf-and-dumb sign language, he was told that this was not an isolated case. Callaway, who according to his father was deaf and dumb from birth, had ridden a bicycle for more than 30 years, and after six weeks' teaching by his father had passed his driving test at the first attempt in 1956. Since then he had driven 6,000–7,000 miles with no trouble. He had learnt deaf-and-dumb language at the age of 17 but had since forgotten it.

No statistics are kept on the number of deaf-and-dumb drivers, because this disability is not one of those specified in the driving licence application forms. On test the examiner's instructions are conveyed either in writing or through an interpreter.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on October 16 the degree of B.M. was conferred on F. S. Plumpton, G. O. M. Jones, and (in absence) on Gillian M. Shaw.

UNIVERSITY OF CAMBRIDGE

In Congregation on August 2 the following degrees were conferred:

M.D.—*Vishnu Sarma.

M.B., B.CHIR.—*I. F. M. Buchanan, R. C. L. Fenciey, *J. G. Lancaster. M.B.—*I. D. Hunter-Craig, N. W. Oakley, J. C. Twomey, *W. G. Shakespeare, A. F. Fleming, J. Hedley-Whyte, A. C. Smith, *A. J. Earl, G. C. Sutton, N. E. S. Holden,* *E. P. Brooks, I. Chippendale, R. H. Johnson, H. B. Valman, *A. Reynolds, D. A. Birkett, F. T. Brough, G. M. Davies, *P. J. Ball, D. M. Whiteford, *Shirley A. Bolt, *Heather M. Rumsey, *Nerys Davies, *Margaret R. Skelton, Mrs. Audrey E. Fairey.

*By proxy.

UNIVERSITY OF ABERDEEN

At a graduation ceremony held on November 5, the degree of M.D. was conferred on H. G. Richmond (with honours) and on R. S. Crow (with commendation).

UNIVERSITY OF DURHAM

In Congregation on September 27 the following degree and diplomas were conferred:

PH.D. IN MEDICINE.—Israel Kleinberg (*In absentia*).

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—J. R. B. Ball, N. E. Crumpton, S. L. Davies, A. King, P. Roughead.

UNIVERSITY OF LONDON

The following have been appointed or nominated for appointment or reappointment as representatives of the University on the governing bodies indicated in parentheses: Dr. R. A. Shooter (Mitchell City of London Educational Foundation) and Dr. Sybil Yeates (Waverley, Burrage, Church Manorway and King's Warren London County secondary schools).

The following have been recognized as teachers of the University in the subjects indicated in parentheses: *St. Mary's Hospital Medical School*, Dr. Michael Feiwel (Dermatology). *London Hospital Medical College*, Dr. G. P. Fox (Anaesthetics), Dr. R. S. Murray (Radiology) and Dr. Richard Creese (Physiology). *Institute of Ophthalmology*, Mr. C. A. G. Cook (Ophthalmology). *Institute of Child Health*, Dr. R. W. Cope (Anaesthetics). *Institute of Orthopaedics*, Dr. P. G. Walker (Biochemistry).

The Sir William Dunn Scholarship for 1958 has been awarded to David Edward Jewitt (King's College).

On August 6 the degree of M.D. was awarded to G. G. Meynell and A. Paton.

The following candidates at the London School of Hygiene and Tropical Medicine have been approved at the examination indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN PUBLIC HEALTH.—L. Baldacci, J. L. Bose, J. M. Davies, R. O. M. Jones.

UNIVERSITY OF BIRMINGHAM

The following appointments have been made: Drs. A. Glass and A. W. Rogers, Lecturers in Anatomy; Drs. H. A. Ellis and D. J. Parish, Lecturers in Pathology; Dr. J. D. Cumming, Lecturer in Physiology; Dr. S. H. Taylor, Lecturer in Medicine; Mr. G. T. Watts and Mr. F. Ashton, Lecturers in Surgery; Dr. E. M. Little, Lecturer in Obstetrics and Gynaecology; Dr. June K. Lloyd, Research Fellow in Paediatrics and Child Health.

UNIVERSITY OF LIVERPOOL

In Congregation on September 26 the degrees of M.B., Ch.B. were conferred on Malvina Harris.

UNIVERSITY OF LEEDS

The following have been approved at the examination of the degree of Ph.D. in the subjects indicated in parentheses: R. Fielden and R. D. Robson (Pharmacology), G. N. Graham (Medicine), and R. Wilson (Experimental Pathology and Cancer Research).

UNIVERSITY OF SHEFFIELD

Dr. Helen Beladi has been appointed full-time research assistant in virus diseases, and Dr. P. Chowdhuri full-time research assistant in the department of obstetrics and gynaecology.

The following resignations have been received: Dr. L. Robertson, honorary demonstrator in bacteriology; and Dr. K. D. Neame, lecturer in physiology.

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At a quarterly comitia of the College, held on October 30, licences to practise were conferred upon the following 136 candidates who had passed the final examination in medicine, surgery, and midwifery of the Conjoint Board and who had complied with the by-laws of the College:

J. W. Abrams, O. O. Akinkugbe, J. G. Allardice, A. C. Ames, E. C. Ashby, Mary E. Ashworth, R. M. Avati, Judith M. Babb, J. R. Ball, N. S. Bamji, F. Bannerman-Lloyd, Anne P. Barrett, Patricia A. Blackwell, Ingrid J. Booth, Helen D. Bower, N. A. Boyd, P. P. Bricknell, M. F. H. Bush, J. S Cameron, M. I. D. Cawley, M. Charlesworth, R. K. Clarke, L. J. Clein, R. J. Clement, Diana E. Clough, G. F. Cohen, L. Cook, S. Craske, A. N. Cruickshank, J. O. Dalrymple, D. J. C. Davies, E. T. L. Davies, J. B. Davis, W. R. Dean, Alison J. Dow, J. T. K. Duncan, A. Dunnill, N. J. Ll. D'Vaz, Margaret L. E. Eastcott, D. R. Edbrooke, Davnet A. V. Fenton, Frances E. Freeman, A. J. V. H. French, A. J. Gardner, Elzbieta E. Gielniewska, A. V. Gillespie, G. T. Gooding, Judith M. Hall, J. W. Harcup, G. Hass, R. T. Hawley, B. Hayes, V. N. Highman, O. Holmes, J. M. Howell, Mary S. Howell, Doreen M. Hudson, Margaret J Hunter Rowe, T. A. Hussell, P. B. Jacobs, R. W. James, Rosemary A. Johnson, O. P. Jones, Mary O. Joseph, P. M. Katrak, C. W. Keen, A. Kenyon, Angela R. Kosky, M. J. S. Langman, M. I. Leckie, J. P. Lee-Potter, L. A. Lees, Valerie Little, L.-S. S. Lung, K. H. McCraith, G. W. McKenna, B. W. Maitland, R. Marks, Sylvie Marston, Margaret Masterton, Ann R. Matthews, T. S. Matthews, N. S. S. Meimary, Yvonne M. Metcalf, D. J. O. Mills, P. V. Mills, D. F. Munro, Janet A. Napper, J. L. Nimmo, R. F. Norris, J. B. Nuttall, J. O. Onyeachonam, A. A. Osindero, Mary W. Parry, P. G. Parry, P. O. D. Pharoah, J. W. Porter, A. C. Pugh, H. B. Raeburn, T. Ramsamy, Marjory M. R. Reid, N. A. Rety, A. B. Richards, G. A. Richardson, R. M. Ridsdill-Smith, Gwyneth M. Riley, R. R. Roberts, Hildegard M. I. Seeman, Olive P. Sharp, Muriel A. Shiel, R. M. Simons, Cynthia G. Smith, I. S. Smith, S. Spragge, Shirley H. Stanness, J. F. Steele-Perkins, Hazel G. Stephens, M. P. Sternberg, D. J. Steward, J. D. M. Stewart, D. W. B. Summers, J. L. K. Tamakloe, Veronica Thatcher, M. J. A. Thompson, R. A. Thompson, M. K. Tidman, J. M. Todd, E. W. B. Varley, S. O. Wamuo, K. H. Warden, J. B. Warren, T. P. Welch, M. P. Wilderspin, M. C. T. Wilkes, G. E. Winbolt, Yvonne Young.

Diplomas in Ophthalmology were granted, jointly with the Royal College of Surgeons of England, to R. J. M. Boucherat and to the other successful candidates whose names are printed below in the report of the meeting of the Royal College of Surgeons of England held on October 9.

Diplomas in Child Health were granted, jointly with the Royal College of Surgeons of England, to Margaret S. Brothwood and R. B. Razvi and to the other successful candidates whose names are printed below in the report of the meeting of the Royal College of Surgeons of England held on October 9.

Diplomas in Industrial Health were granted, jointly with the Royal College of Surgeons of England, to M. C. Gupta and P. V. Krishnamurti.

Diplomas in Tropical Medicine and Hygiene and in Physical Medicine were granted, jointly with the Royal College of Surgeons of England, to the successful candidates whose names are printed below in the report of the meeting of the Royal College of Surgeons of England held on October 9.

Other diplomas were granted, jointly with the Royal College of Surgeons of England, as follows:

DIPLOMA IN PUBLIC HEALTH.—D. S. Jani.

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—G. Woolfson.

DIPLOMA IN ANAESTHETICS.—D. M. Davies.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on October 9, with Sir James Paterson Ross, President, in the chair, the Mitchiner Medal was presented to Lieutenant-Colonel R. H. Robinson by the Director-General of the Army Medical Services (Lieutenant-General Sir Alexander Drummond).

The Handcock Prize was presented to Mrs. E. M. Cooke, of the Royal Free School of Medicine.

Mr. F. R. Jackaman (Queen Elizabeth's School, Barnet, and Cambridge University) was admitted as Macloghlin Scholar.

The John Hunter Medal and Triennial Prize were awarded to Dr. L. W. Proger, Pathology Curator, for his devoted services to the Hunterian Museum.

The award of a Mackenzie Mackinnon Research Fellowship to Mr. K. E. D. Shuttleworth was announced.

Arrangements were approved for the celebration next year of the centenary of the institution of the licence in dental surgery.

A diploma of Fellowship was granted to B. P. Scrivener, and a diploma of Membership to A. B. Richards.

Diplomas of Fellowship in the Faculty of Anaesthetists were granted to the following successful candidates:

Jean M. Horton, S. W. Kemp, B. R. J. Simpson, J. D. K. Burton, T. M. McAneny, A. McL. Keil, Patricia Painter, R. L. Hargrove, T. M. Ness, S. Thirumalai, J. L. Hadley, Ellen R. S. Armitage, A. J. Booth, Sheila R. Clarke, B. J. Muir, J. R. Munro, B. Solomon, F. R. Bhupalan, F. S. Keddie, R. M. Nicholl, T. J. Stanton, G. Tay, H. R. P. Coutanceau, G. W. Duckworth, G. L. F. Lau, F. M. Mehta, I. A. Sloan, J. V. Farman.

The following diplomas were granted, jointly with the Royal College of Physicians of London:

DIPLOMA IN OPHTHALMOLOGY.—A. K. Banerjee, J. C. Chang, K. K. Chau, S. R. Chowdhuri, B. P. Cooper, R. J. Croke, Elizabeth L. R. Douglas, L. K. Dutta, J. M. Elsby, Asuncion N. Fernando, R. S. Garkal, J. H. Li George, P. K. Ghosh, Elizabeth F. Hamilton, A. C. A. Hempel, D. E. Hone, M. I. Khan, S. Khoshnevis, A. Krishna Murthy, P. Lancer, M. G. Lyall, A. J. Lyne, A. Lytton, K. J. Modi, V. S. Pande, M. V. Parikh, J. A. Pearce, H. J. Penkala, Pe Than Maung, D. N. Randeria, J. M. Rodd, P. G. Rowsell, I. S. Roy, M. L. Sharma, S. A. Sheikh, G. E. M. Smith, G. C. Sood, D. J. Thornton, N. H. Welsh, G. S. Willetts, M. S. Wilson.

DIPLOMA IN CHILD HEALTH.—V. K. Agarwal, V. C. Agarwal, Hilary Allin, Elizabeth M. F. Andrews, K. D. Austin, J. F. Baden-Daintree, S. Barua, N. Bhaktilingam, Josephine Bradford, Helen R. L. Brown, K. W. Browne, Anne J. Burge, Mary S. Campbell, J. C. Chakrabarti, C. P. Chin, D. R. Chopra, R. K. Chopra, J. Connolly, M. J. Conway, Izette R. Coulton, P. N. Cretney, Edith Danos, B. S. David, G. N. Dubey, V. Dubowitz, F. M. Elderkin, J. H. Fairley, Hazel M. Fearn, W. R. Forbes, R. A. Gould, Margaret S. Hall, Jean G. Harrison, I. A. Hashimi, Anne Heath, C. P. Hindley, Barbara L. Hooker, M. J. Howell, D. Hull, Rosemary Hulley, J. A. Inall, S. Isaac, Wilma J. Israelsohn, Celia A. James, G. W. Johnston, J. Keane, Katie Keane, P. N. Krishnamurthy, Julie S. S. Lim, H. M. Lipman, Gwendolen Mallal, A. V. Mar, Valerie J. Marrian, W. C. Marshall, A. P. Mayne, G. K. Mehrotra, H. S. Memon, A. K. Miller, A. Mithal, D. M. Morgan, Khursheed Moulvi, Janice H. Mount, J. E. Newcombe, Heather B. Nunnerley, Susan B. G. Ofori-Atta, J. P. O'Neill, M. S. Pardiwalla, K. M. Patel, P. Pitney, Norah T. E. Power, H. V. Price, Ann Priestman, Gillian Prosser-Ashby, K. A. Rahimtulla, Shirley G. Ratcliffe, L. Sash, R. Schofield, S. Shabbir, Jean Shackleton, A. J. H. Shepherd, K. Soni, Anne L. Stewart, Susan Stonestreet, M. K. Strelling, Margaret J. D. Sturges, Hui Lim Helen Tay, A. F. Taylor, Dileas M. Tingle, H. L. Utian, N. A. Vellani, Geraldine M. Walshe, K. Warburton, R. W. Watton, Mary Wilkie, R. Winstone, Lina Yut Lin Yong.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—S. Abedin, A. A. A. Ahmed, K. Bery, F. S. Boi-Doku, M. C. Brain, K. R. Bremner, D. G. Carlson, Hin-Wing Chan, D. P. Daly, M. E. Fearnley, R. D. Foord, D. A. Gandhi, D. J. Hansman, T. Htun, H. A. Jesuthasan, B. Jha, H. A. F. V Kassam, H. J. Khambatta, M. A. Khan, M. D. Khan, K. K. Korsah, M. C. Latham, P. B. Lees, M. H. Mahmoud, K. K. Mallik, M. A. Mannan, F. X. Martin, M. C. Mathews, R. A. Miller, D. Misra, M. T. Moore, H. Nadjy, Rosemary A. Page, G. M. J. Pais, Valerie J. Prior, S. H. Qureshi, W. H. Rees, S. P. Shah, J. Sharan, R. P. Singh, R. Singh, D. R. Stein, B. V. Suryanarayana, N. A. Syed, I. Taha, Tha Khin, T. Thavornsiri, E. Trinick, K. E. Ussher, N. A. Vellani, C. Vesuna, A. E. Wanigesooria, Anje Wiersinga, M. H. Zafar.

DIPLOMA IN PHYSICAL MEDICINE.—E. N. Coomes, R. Danbury, Helene V. Goodman, G. Holden, K. H. Nixon, S. K. Sarkar, V. L. Steinberg, W. G. Wenley, V. B. Whittaker.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

At the annual meeting of Fellows, held on October 18, the following officers were appointed for 1958-9: *President*, Dr. P. T. O'Farrell; *Vice-President*, Dr. M. Crowe; *Representative of College on General Medical Council*, Dr. Edward T. Freeman; *Registrar*, Dr. Charles Dickson; *Treasurer*, Dr. Geoffrey Bewley.

ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

At a meeting of the Council of the College held in Melbourne on October 9 the following candidates, who were successful at an examination by the Australian Board of Censors, were admitted to Membership of the College: Dr. W. Berns, Dr. F. J. T. Croll, Dr. J. C. Farrell, Dr. H. G. Gallagher, Dr. B. R. Huxtable, Dr. K. P. W. Moore, and Dr. T. Selby, of New South Wales; Dr. N. McK. Bennett, Dr. R. A. Chenoweth, Dr. A. E. Doyle, Dr. A. D. Grounds, Dr. F. L. Johnson, Dr. D. S. Nurse, Dr. R. G. Shaw, Dr. L. E. G. Sloan, Dr. B. M. Spence, Dr. J. B. Webb, and Dr. C. W. E. Wilson, of Victoria; Dr. B. J. Knapp and Dr. J. P. Masel, of Queensland; Dr. I. J. Forbes and Dr. J. G. Wilson, of South Australia. Dr. J. A. Bonnin, of South Australia, and Dr. K. V. Smith, of New South Wales, were admitted under the special provisions of Article 37.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **October 25** (No. 43) and corresponding week 1957.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included). London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	4	3	6	0	2	3	0	4	0	
Dysentery	525	61	157	5	2	197	20	89	1	4
Encephalitis, acute	6	0		0		2	0		1	
Enteric fever:										
Typhoid ..	3	0	0	0	2	4	0	0	2	
Paratyphoid ..	10	0	6(B)	0	8(B)	1	0	0	0	
Food-poisoning ..	228	33	15	7		108	16	84	0	
Infective enteritis or diarrhoea under 2 years				12	53				4	38
Measles*	4,232	243	28	53	205	1,414	23	24	27	19
Meningococcal infection	29	3	14	0	1	35	7	12	1	2
Ophthalmia neonatorum	26	4	10	0		35	4	5	0	
Pneumonia† ..	263	21	164	13		1,897	138	622	47	67
Poliomyelitis, acute:										
Paralytic ..	62	6	26	3	5	56	3	3	4	3
Non-paralytic ..	13	0				10	0			
Puerperal fever.§ ..	212	38	15	1		287	34	5	1	
Scarlet fever ..	803	56	106	27	51	399	40	64	13	32
Tuberculosis:										
Respiratory ..	481	58	81	19		515	56	113	20	
Non-respiratory	53	4	8	3		74	8	11	2	
Whooping-cough ..	594	36	69	67	34	349	22	22	0	11

DEATHS	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0	0	No comparable figures available.	0	0	0	0
Dysentery	0	0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever ..	0	0	0	0			0	0	0	
Infective enteritis or diarrhoea under 2 years	6	0	2	1	0		0	0	0	0
Influenza	13	3	1	0	0		51	31	16	13
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	0				3	1		
Pneumonia ..	422	28	18	15	3		76	24	31	8
Poliomyelitis, acute	4	1		0	0		1		0	0
Scarlet fever ..		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	72	5	6	0	5		9	12	1	8
Non-respiratory		0	1	0	1		0	3	0	0
Whooping-cough ..	0	0	0	0	0		0	0	0	0
Deaths 0–1 year ..	321	23	26	6	10		32	22	3	5
Deaths (excluding stillbirths) ..	9,056	751	539	104	134		955	647	138	190
LIVE BIRTHS .	13,874	1141	1005	222	344		1243	992	197	317
STILLBIRTHS .	307	27	17				25	18		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

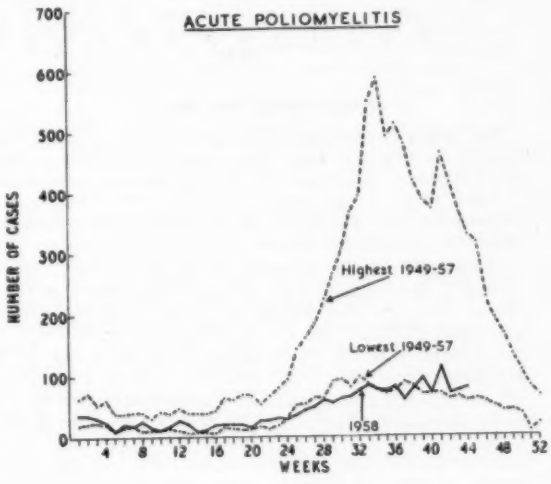
Vital Statistics

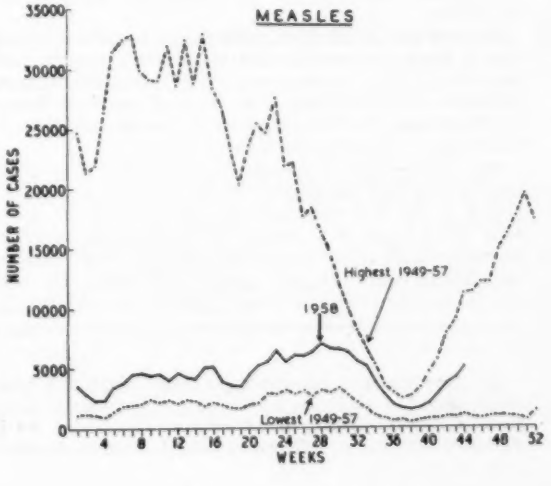
Typhoid : Oysters Suspected

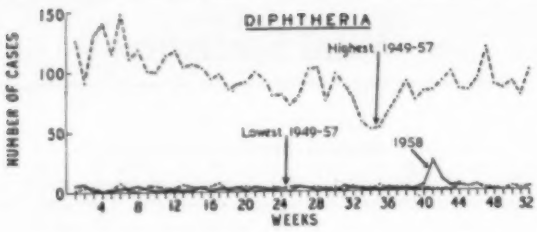
Seven cases of typhoid fever suspected of being caused by infected oysters have been reported recently. They are in the London area, except for one at Sidcup, Kent, and one at Sudbury, Suffolk. The last patient ate the oysters in Colchester, Essex, the others in London. In three cases the oysters are known to have come from the West Mersea beds, and in four cases the West Mersea strain of the bacillus has been identified.

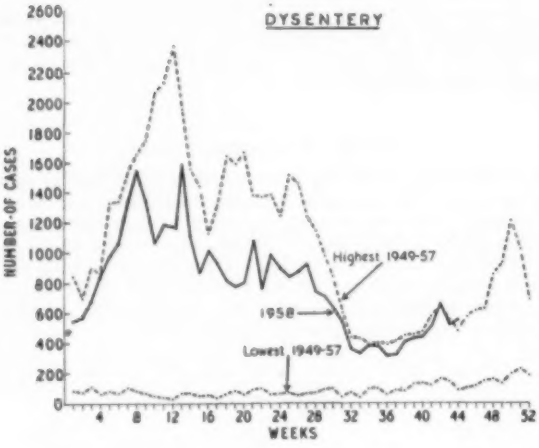
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus ------, the figures for 1958 thus ————. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending November 1

The largest fluctuations in the notifications of infectious diseases in England and Wales during the week ending November 1 were increases of 782 for measles, from 4,232 to 5,014, 86 for scarlet fever, from 803 to 889, 53 for acute pneumonia, from 263 to 316, 43 for whooping-cough, from 594 to 637, and 26 for dysentery, from 525 to 551.

The largest rises in the incidence of measles were 155 in Yorkshire West Riding, from 461 to 616 (Halifax C.B. 167), 106 in Yorkshire East Riding, from 195 to 301 (Kingston-upon-Hull C.B. 263), 88 in Lincolnshire, from 165 to 253 (Scunthorpe M.B. 83), 87 in Surrey, from 60 to 147, 82 in Middlesex, from 200 to 282, and 79 in Sussex, from 82 to 161; the largest falls were 68 in Caernarvonshire, from 134 to 66, 56 in Devonshire, from 169 to 113, and 49 in Hampshire, from 101 to 52. Only small changes in trend were reported in the local areas for scarlet fever and whooping-cough. 6 cases of diphtheria were notified, being 2 more than in the preceding week; 3 of these cases were notified in London.

The notifications of acute poliomyelitis numbered 79 and were 8 fewer for paralytic and 12 more for non-paralytic cases than in the preceding week. The largest returns were Lancashire 19 (Manchester C.B. 9), Yorkshire West Riding 12 (Nidderdale R.D. 6), Durham 5 (Sunderland C.B. 2), Hampshire 5 (Southampton C.B. 2), London 5.

The chief centres of infection for dysentery were Yorkshire West Riding 100 (Leeds C.B. 44), Lancashire 53 (Liverpool C.B. 20), Glamorganshire 52 (Cardiff R.D. 22, Barry M.B. 12), London 46 (Islington 10, Wandsworth 10), Northumberland 32 (Newbiggin-by-the-Sea U.D. 19), Warwickshire 25 (Coventry C.B. 16); Essex 24 (Walthamstow M.B. 14), Hampshire 23 (Southampton C.B. 18), and Durham 22.

The New Zealand Department of Health (P.O. Box 5013, Wellington) has published a *Directory of Homes and Clubs for Old People*. This is based on a survey carried out in February last, and it is hoped to publish supplements from time to time.

Medical News

Epsom College Scholarships.—The council of Epsom College will, about the end of May, 1959, elect to one or more Henry Robinson scholarships, tenable from September, of a maximum value of £250 a year. These scholarships are open only to sons of registered medical men or women, aged between 12 and 14 on January 1, 1959. They are awarded on the results of a competitive examination, and there is no means test. About 5 or 6 open scholarships will be given on the results of the same examination, maximum value £150 a year; for these, boys of medical parentage compete on level terms with sons of the laity. Full details can be obtained from the Headmaster, Epsom College, Epsom.

Royal College of Obstetricians and Gynaecologists.—A large gathering of obstetricians and gynaecologists, their guests, and their ladies attended the College's annual dinner at the Dorchester Hotel on November 7. The president, Professor ANDREW CLAYE, was in the chair, and after the dinner and speeches there was dancing. Sir MALCOLM TRUSTRAM EVE, Q.C., First Crown Estate Commissioner, welcomed the College as new tenant of the Crown in Regent's Park. It was the desire of the Crown Commissioners to save all the Nash terraces if possible, he said; each building facing the park would revert to residential use, and each terrace would be largely rebuilt, but retaining, or returning to, Nash's original elevation. The College was privileged in being allowed to build its new house in what is a "residential area," and Sir Malcolm expressed the hope that some other colleges might join them there. Professor CLAYE, responding, said the building was progressing steadily and should be finished by the end of 1959. While they could now see enough money forthcoming to build and equip it, funds for its maintenance were still urgently needed. It would become the focal point of almost all their work. The College, he continued, was engaged, with the help of its councils in the Dominions, in revising the M.R.C.O.G. Extramurally, it was taking part with other bodies in the review of the N.H.S. and in other matters of professional concern. Dr. T. F. FOX, for the guests, replied to Mr. JOHN PEEL'S gracious toast: the evening, he said, had been positively Caesarean.

Doctors' Hobbies.—The second Doctors' Hobbies Exhibition, organized by Benger Laboratories Ltd., was opened on November 10 by Sir CLAVERING FISON, chairman of the Fison Group, in the Great Hall of B.M.A. House. More than 500 doctors showed samples of the things they do in their leisure time, to make an impressive collection of over 700 exhibits. First prize was won by Dr. A. W. FAWCETT, of Sheffield, whose 4 ft. model of the torpedo-boat destroyer *Tigress*, in which he served, had taken him 14 years to complete. The second prize went to Dr. A. H. WORTMAN, of London, for a collection of stamps issued by Imperial Russia in 1858. Dr. S. COMPTON, of Guildford, took the third prize for tapestries of exceptional quality. The exhibits were grouped in 23 classes, of which easily the most popular were those for photography (transparencies, portraiture, and general) and painting (oil and watercolour). Next in popularity were "authorship," embroidery, woodwork, and sculpture and wood-carving. But such a list gives little idea of the great variety of the profession's leisure interests: they include, for instance, tame chinchillas, popular songs, stage properties, Esperanto, the collection of abbreviations from newspapers and journals, poetry, an electronic organ, sock-darning, a telephone-tapping device, ships in bottles, models of all kinds, ceramics, violins, and match-box labels. The standard was far higher than last year, and once again the photographs were outstanding. The paintings were more numerous and included some fine work, notably the prize-winning industrial landscapes by Dr. A. B. FOLLOWS and Dr. PH. TUTTNAUER'S imaginative "Boats at Rest." The exhibition was open for five days.

Transatlantic Clinical Conference.—The British panel for the transatlantic clinical conference on December 5 between the B.M.A. Annual Clinical Meeting in Southampton and the A.M.A. Meeting in Minneapolis, U.S.A., will be Dr. W. D. BRINTON (chairman), Professor JOHN MCMICHAEL, F.R.S., and Mr. HOLMES SELLORS. The Clinical Meeting, which lasts from December 4 to 7, will also include four panel discussions and three general sessions on practical clinical subjects. Advance registration forms for the meeting are obtainable from the Executive Officer, B.M.A. House, Tavistock Square, London, W.C.1. These should be completed and returned without delay.

London Medical Exhibition.—Sir ROY CAMERON, F.R.S., gave the address at the opening of the 42nd London Medical Exhibition, held at the Royal Horticultural Hall, Westminster, from November 10 to 14. The exhibition is staged each year by the British and Colonial Druggist Ltd. Pride of place at the exhibition, said Sir Roy, went to treatment. Doctors would find new measures for the more effective use of healing drugs, not only by prolonging their local and general action and removing unpleasant side-effects but by promoting their absorption, simplifying their administration, and, above all, by doing away with even the remote possibility of danger. No less important was reduction in cost, something that must appeal to everyone in these days of financial stringency. It was fitting, too, that new discoveries in the recognition of disease should be placed as early as possible before the profession, and the London Medical Exhibition had certainly accepted its responsibilities in that direction. Simpler apparatus for blood-pressure determination, reliable stains for microscopical diagnosis, and less complicated methods for examination of the urine, blood, and body excretions would appeal to those who spent their lives in the quiet alleys of medical endeavour. As one whose life had been given up to teaching and investigation, he commended this display of the development and application of medical research.

Royal College of Physicians of Edinburgh.—At a quarterly meeting of the College held on November 4, 1958, with the president, Dr. A. RAE GILCHRIST, in the chair, the following were elected Fellows of the College:

F. P. Reid, Maung E, K. N. Gour, R. Schneider, T. Schneider, I. Singh, N. Ali, I. Schrire, H. A. Reid, J. M. Staveley, G. B. Tait, M. Watt, S. G. Nelson, G. M. Carstairs, J. N. Swanson, D. H. Clark, M. A. Keith, A. C. Bhabha, N. C. Begg, R. Grenville-Mathers, A. M. Kassim, S. R. K. Padmavati, J. D. Matthews, P. C. Mitchell, J. F. McHarg, S. E. Large, W. S. Watson, J. Harper, W. Macleod, M. Macleod, H. B. Craigie, S. P. V. Sherlock.

The following were elected Members of the College:

D. F. Cappell, D. M. Fraser, W. M. Millar, K. M. Robertson, K. S. Grover, F. R. D. Minett, P. K. Roy, M. O'Mahony, R. D. Spooner, S. N. Mukherjee, E. T. Hughes, D. J. Hodges, J. C. Ghosh, J. G. Sowerbutts, S. Janaki, W. A. Penman, A. M. Womack, N. S. Dhillon, E. C. Knox, P. V. Vora, S. G. F. Matts, M. D. Kay, L. L. Sinha, S. S. Syalee, E. S. Emslie, D. Montgomery, T. D. Grant, G. P. McGovern, C. E. Rotem, T. K. Chaudhuri, T. C. Dennison, P. S. Terespolsky, P. C. Sharma, D. J. Robinson, S. V. Bakshi, A. J. Watson, S. S. Jhaveri, G. W. Ashcroft, J. S. Beck, W. K. C. Morgan, E. J. Raffle, J. R. Tighe, P. Ganeriwala, J. A. Fuller, H. R. Klein, O. P. Gupta, I. W. Delamore, A. Mitra, J. Dominian, E. Chesler.

Royal Faculty of Physicians and Surgeons, Glasgow.—Besides the election of Mr. A. H. Jacobs as president (*Journal*, November 8, p. 1171), the following were elected office-bearers at the annual general meeting of the Royal Faculty of Physicians and Surgeons of Glasgow on November 3: Visitor, Dr. J. H. Wright; hon. secretary, Dr. Gavin B. Shaw; hon. treasurer, Mr. R. B. Wright; hon. librarian, Dr. A. L. Goodall; representative on the G.M.C., Dr. Andrew Allison; councillors, Dr. G. J. Aitken, Dr. W. Ferguson Anderson, Dr. W. Malcolm Gibson, Dr. D. McKay Hart, Dr. A. Cameron Macdonald, Dr. T. J. Thomson, and Professor G. M. Wyburn. Dr. C. G. A. Thomas was presented with a cheque for his winning essay in a competition sponsored by the council of the Faculty for the trustees of the Glasgow Lock Hospital Fund.

Poisons List.—The Home Office announces that Statutory Instruments are being prepared to give effect to recommendations from the Poisons Board. It is proposed to make the following changes in the Poisons List and Rules:

1.—Anileridine, dextromoramide, etoxeridine, levomoramide, methyldihydromorphine, morpheridine, myrophine, oxymorphone, racemoramide, trimeperidine, and the esters of 1-methyl-4-phenylpiperidine-4-carboxylic acid, and the salts of these substances, will be added to Part I of the Poisons List and the First Schedule to the Poisons Rules. The existing entries relating to pethidine and the isopropyl ester of 1-methyl-4-phenylpiperidine-4-carboxylic acid and their salts will be deleted.

2.—Derivatives of 3-(10-phenothiazinyl) propane substituted in the 1-position, and the salts of these substances, will be added to Part I of the Poisons List and to the First and Fourth Schedules to the Poisons Rules. The existing entries relating to chlorpromazine and promazine and their salts will be deleted.

3.—Endrin will be added to Part II of the Poisons List and to the First, Fifth (in respect of "preparations for use in agriculture or horticulture"), Seventh, Eighth, and Ninth Schedules to the Poisons Rules.

4.—2-Methoxycarbonyl-1-methylvinyl dimethyl phosphate ("phosdrin") will be added to the list of phosphorus compounds in Part II of the Poisons List, in Rule 14(2)(b)(vi) of the Poisons Rules and in the First, Third, Fifth, Seventh, Eighth, and Ninth Schedules. It will also be added to the Sixteenth Schedule.

5.—Organic compounds of mercury in aerosols will be included in the First Schedule to the Poisons Rules regardless of their percentage content of mercury, and also in paragraph 6 of the Seventh Schedule.

6.—The entry in the second column of the Fifth Schedule to the Poisons Rules relating to calcium arsenates will be amended to read "preparations for use in agriculture or horticulture."

7.—The requirement in Rule 12(2)(e) and (f) of the Poisons Rules that a prescription for a poison included in the Fourth Schedule shall show the total amount to be supplied or the total amount intended to be administered or injected will be amended to exclude preparations included in the *British National Formulary*.

Central Midwives Board Headquarters.—The MINISTER OF HEALTH, accompanied by Mrs. WALKER-SMITH, officially opened the new offices of the Central Midwives Board during a reception held in the new building, at 39, Harrington Gardens, London, S.W.7, on November 6. The Board has taken a 64-year lease of the house, which provides enough accommodation for its increasing work. Last year there were 4,039 successful candidates for the first part of the midwives certificate examination, and the names of 2,800 women were enrolled on the register as having been successful in the second part. The chairman of the Board, Dr. ARNOLD WALKER, and Mrs. WALKER received the guests at the reception.

Birmingham University.—The title of reader in comparative neurology has been conferred on Dr. J. T. EAYRS, senior lecturer in neuro-anatomy and at present Henry Head research fellow of the Royal Society in the department of anatomy. Dr. H. A. SALMON has been appointed a temporary lecturer in physiology, and Dr. B. J. KEY a research fellow in the department of experimental psychiatry.

N.E. Metropolitan Board.—Sir JAMES PATERSON ROSS, P.R.C.S., was the principal guest at the eighth annual dinner of the North-east Metropolitan Regional Hospital Board on October 22. Over 300 attended, under the chairmanship of the Board's chairman, Sir GRAHAM ROWLANDSON.

St. John Ambulance Brigade.—Mr. G. W. WOODHILL, Cadet Officer for London District since 1955, has been appointed secretary of the Brigade in succession to the late Mr. GEORGE QUILTER.

Professor W. C. W. Nixon has been elected a foreign member of the Turkish Society of Obstetrics and Gynaecology.

COMING EVENTS

University College, London.—Dr. D. A. DENTON, director of the Ion Exchange Research Unit, Melbourne, will lecture on "The Control of Secretion of the Transplanted Adrenal Gland" on November 19 at 5.30 p.m. in the physiology theatre.

Institute of Neurology.—Professor J. N. CUMINGS will deliver his inaugural lecture as professor of chemical pathology at the Institute of Neurology, Queen Square, on November 24 at 5.30 p.m. His subject will be "Neurochemistry and Neurochemists."

Kettle Memorial Lecture.—Dame JANET VAUGHAN will lecture on November 27 at 5 p.m. at St. Bartholomew's Hospital Medical College on "The Relation of Radiation Dosage to Radiation, with Reference to Bone-seeking Isotopes."

Richard Bright Centenary.—On December 1 Guy's Hospital Medical School is celebrating the centenary of Bright's death with a combined round on Bright's disease (2.15 p.m.) and a memorial lecture (5 p.m.) by Professor M. L. ROSENHEIM on "The Syndromes of Bright's Disease." Further details are obtainable from the Medical School.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, November 17

GUY'S HOSPITAL.—At Anatomy Lecture Theatre, 5.15 p.m., lecture demonstration in endocrinology by Dr. P. M. F. Bishop: Acromegaly.

HUNTERIAN SOCIETY.—At Apothecaries' Hall, 8.30 p.m., discussion: This Society Accepts the Need for Human Artificial Insemination. Speakers, Rt Rev. the Lord Bishop of Croydon, Mr. W. A. Fearnley-Whittingstall, Q.C., and Mr. V. B. Green-Armytage.

Tuesday, November 18

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. W. Hayes: Bacterial Genetics and Gene Structure.

HEATHERWOOD ORTHOPAEDIC HOSPITAL.—8.30 p.m., Mr. J. Charnley: Lubrication of Joints, with Special Reference to Arthroplasty.

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. G. C. Wells: Mechanisms of Epidermal Sensitization.

KEIGHLEY AND DISTRICT MEDICAL SOCIETY.—At Skipton General Hospital, 8.30 p.m., Dr. P. C. Reynell: Some Recent Advances in the Treatment of Liver Disease.

MANCHESTER MEDICAL SOCIETY.—At Large Anatomy Theatre, Manchester University, 4 for 4.30 p.m., University Lecture on the History of Medicine by Dr. W. S. C. Copeman: Doctors and Disease in Tudor Times.

MANCHESTER UNIVERSITY: DEPARTMENT OF OCCUPATIONAL HEALTH AND NORTH-WEST ENGLAND FACULTY, COLLEGE OF GENERAL PRACTITIONERS.—At Theatre 1, Clinical Sciences Building, York Place, 8.30 p.m., Professor R. E. Lane: Effect of Work on Some Selected Medical Conditions.

RESEARCH DEFENCE SOCIETY.—At Lecture Theatre, Zoological Society of London, Regent's Park, N.W., 5.30 p.m., 27th Stephen Paget Memorial Lecture by Mr. Richard Fort, M.P.: The Irrational in Public Life.

ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Charles West Lecture by Dr. E. M. Creak: Child Health and Child Psychiatry—Neighbours or Colleagues?

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Mr. J. S. Tompkinson: History and Present-day Practice of Contraception.

UNIVERSITY COLLEGE LONDON.—At Anatomy Theatre, Gower Street, W.C., 1.15 p.m., Mr. D. A. Sholl: Randomness of the Brain.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF PHARMACOLOGY.—At Physiology Theatre, Gower Street, W.C., 5.30 p.m., Professor J. F. Danielli, F.R.S.: Generalized Cell Theory and Its Relevance to Certain Problems of Drug Action.

WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Mr. K. I. Nissen: Carpal Tunnel Syndrome.

Wednesday, November 19

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. J. A. Dudgeon: Virus Diseases.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. V. C. Thompson: Carcinoma of the Lung: Early Diagnosis.

INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. Harland Rees: Differential Diagnosis of Frequency of Micturition.

MIDLAND MEDICAL SOCIETY.—At Dudley Road Hospital, 8.15 p.m., clinical meeting.

●NATIONAL COLLEGE OF RUBBER TECHNOLOGY, Northern Polytechnic, Holloway Road, N.—6.30 p.m., Mr. O. F. Mackinson: Plastics in Dentistry.

NORTH-WESTERN THORACIC SOCIETY.—At Aintree Hospital, Liverpool, 5 p.m., Dr. D. L. Caldwell, Selection of Patients for Admission to a Chronic Bronchitic Unit; Dr. G. Yates, Chronic Bronchitis in General Practice; Dr. M. Davies, Bronchitis and Atmospheric Pollution.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Guest Lecture by Dr. S. M. Cohen: Turnover of Plasma Proteins.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Mr. J. Sharp Grant: Some Comments on the Development of Occupational Medicine. (Illustrated.)

SCIENTIFIC FILM ASSOCIATION.—At 4th Floor Temporary Lecture Theatre, Royal College of Surgeons of England, 6.30 p.m., subject: Presenting Medicine to the Public on Television. Principal speaker, Mrs. Mary Adams. Discussion to be opened by Mr. A. Dickson Wright.

UNIVERSITY COLLEGE LONDON.—At Department of Pharmacology, 5.30 p.m., Dr. D. A. Denton (Melbourne University): The Control of Secretion of the Transplanted Adrenal Gland.

WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Nurses' Hall, West London Hospital, W., 8.30 p.m., Mr. J. Johnston Abraham: The West London 50 Years Ago.

Thursday, November 20

●BRISTOL UNIVERSITY.—At Reception Room of University, 8.15 p.m., Carey Coombs Memorial Lecture by Dr. Bernard Schlesinger: Course and Treatment of Rheumatoid Diseases in Childhood.

BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., subject: Use of the Rad as a Dose Unit in Radiotherapy. To be opened by Dr. F. Ellis, Dr. C. W. Wilson, and Mr. D. E. A. Jones.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Dr. J. H. Humphrey: What are Gamma-globulins?

HONEYMAN GILLESPIE LECTURES.—At Anatomy Theatre, University New Buildings, Teviot Place, Edinburgh, 5 p.m., Professor J. Walker: Foetal Dissociation Curve for Oxygen.

HYPNOTHERAPY GROUP.—At Royal Society of Medicine, 8 p.m., Dr. Peter Scott: Crime and Adolescence.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 4.30 p.m., Guest Lecture by Mr. D. M. Stern: Abnormal Uterine Haemorrhage.

LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Hugh Owen Thomas Memorial Lecture by Mr. H. Jackson Burrows: Prosthetic Replacement of Bone.

MANCHESTER MEDICAL SOCIETY: SECTION OF ANAESTHETICS.—At Staff House, Manchester University, 7.45 for 8 p.m., Presidential Address by Dr. A. J. Gray: On Veins and Needles.

●NEW HEALTH SOCIETY.—At Board Room, Y.W.C.A. Central Club, Great Russell Street, London, W.C., 3 p.m., Mr. T. T. Stamm: Foot Troubles.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At Liverpool School of Tropical Medicine, 7.30 p.m., laboratory meeting.

ST. ANDREWS UNIVERSITY.—At Physiology Department Lecture Theatre, 5 p.m., Dr. Agnes R. Macgregor: Changing Problems of Paediatric Pathology.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. Maurice Partridge: postgraduate demonstration in psychiatry.

UNIVERSITY COLLEGE LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, Gower Street, W.C., 5 p.m., Dr. E. M. Shooter: Configuration of Proteins in Solution.

Friday, November 21

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 5 p.m., 4th Crookshank Lecture by Lord Cohen of Birkenhead: Contribution of *X*-rays to the Basic Medical Sciences.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. D. I. Williams: clinical demonstration.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Mr. J. R. Belcher and Dr. E. H. Hudson: clinical demonstration.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—(1) 3.30 p.m., clinical discussion for general practitioners by Mr. Maxwell Ellis: Malignant Diseases of the Pharynx. (2) 5.30 p.m., demonstration of films by Dr. T. V. L. Crichlow.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Hospital 2 p.m., Guest Lecture by Mr. D. McKay Hart: Virus Diseases Complicating Pregnancy.

LEICESTER CHRISTIAN MEDICAL ASSOCIATION.—At Leicester Royal Infirmary, 8.45 p.m., Dr. Robina A. Taylor (Ghana): Racial Problems in Medical Practice.

●MIDLAND CENTRE FOR NEUROSURGERY, Holly Lane, Smethwick.—8 p.m., Sir Russell Brain: Endocrine Exophthalmos.

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—10 a.m., Guest Lecture by Mr. T. Holmes Sellors: Diagnosis and Treatment of Atrio Septal Defects.

Saturday, November 22

SCOTTISH OTOLARYNGOLOGICAL SOCIETY.—At Royal Infirmary, Dundee, 2 p.m., 77th meeting.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Naylor.—On October 28, 1958, at Ann Arbor, Michigan, U.S.A., to Paz Buenaventura (formerly Dominado) and Bernard Naylor, a son—Patrick John.

Winter.—On October 18, 1958, to Dr. Margery Joan, wife of Dr. David Winter, 292, Hagley Road, Birmingham, a daughter—Sarah Elizabeth.

DEATHS

Cohen.—On October 23, 1958, at 35, Bath Hill Court, Bournemouth, Jack Cohen, L.R.C.P.&S.I., of Southport.

Coulson.—On October 21, 1958, at a nursing-home, James Edmund Coulson, M.R.C.S., L.R.C.P., aged 92.

Galloway.—On October 20, 1958, at Castle Street, Banff, John Charles Galloway, M.D., D.P.H., aged 82.

Hay.—On October 19, 1958, at Stoncham, The Mall, Brading, Isle of Wight, Arthur Edgar Hay, M.R.C.S., L.R.C.P., aged 80.

Hughes.—On October 19, 1958, at 20, Broomfield Lane, Hale, Cheshire, Thomas Martin Hughes, M.R.C.S., L.R.C.P., L.D.S. R.C.S., aged 80.

James.—On October 15, 1958, at Gateacre Grange, Liverpool, Dorothy Mary James, M.D., D.P.H., aged 54.

Jenner.—On October 22, 1958, Cyril William Jenner, L.M.S.S.A., of Mortimers, Manningford Bohune, Wilts, late of Cherrimans, Shottermill, Haslemere, Surrey.

Knight.—On October 19, 1958, at 162, Willesden Lane, London, N.W., Stephen John Knight, M.R.C.S., L.R.C.P.

Macdonald.—On October 21, 1958, at Harpenden Memorial Hospital, Herts, William George Macdonald, M.B., Ch.B. (1908).

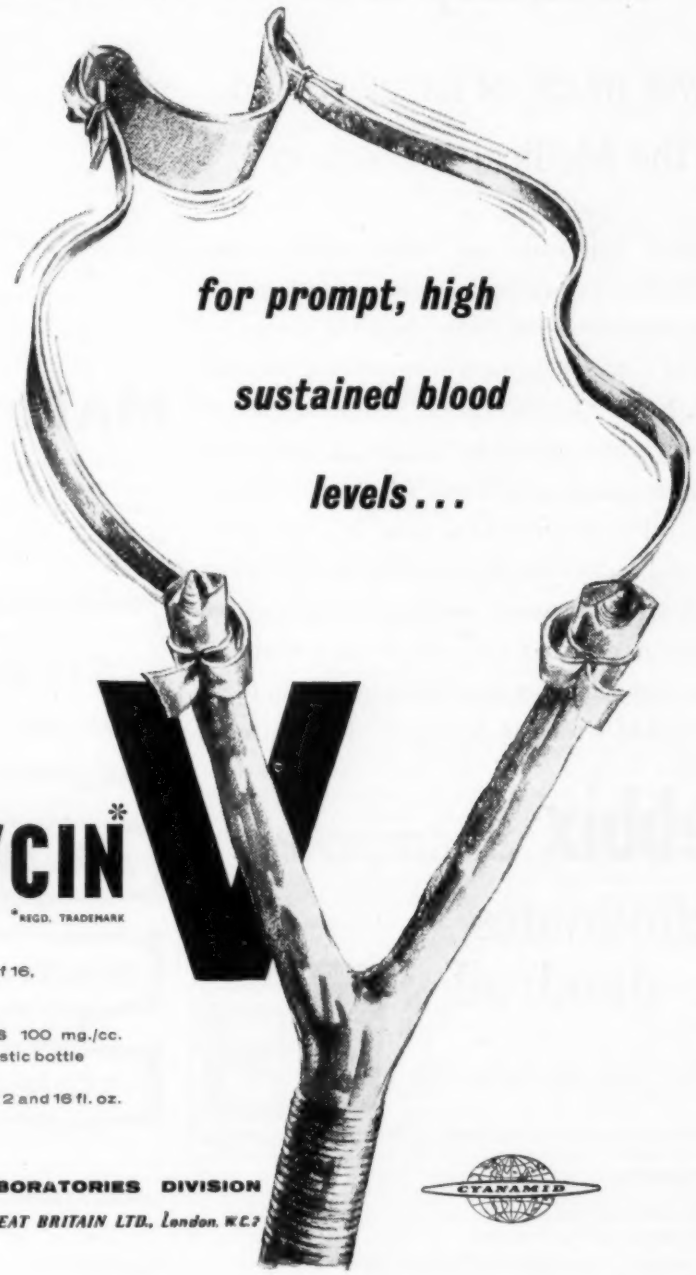
Thomas.—On October 20, 1958, Arthur Henry Thomas, M.B.E., M.B., Ch.B., aged 84.

Todd.—On October 20, 1958, Arthur Theodore Todd, O.B.E., M.B., Ch.B., of Upton Cheyney, Bitton, near Bristol.

Wilson.—On October 21, 1958, John Stephen Herbert Wilson, M.R.C.S., L.R.C.P., of Old Forge House, Hatfield Broad Oak, Bishop's Stortford, Herts.

CATAPULTED

into high favour



for prompt, high sustained blood levels . . .

ACHROMYCIN*

BUFFERED TETRACYCLINE

*REGD. TRADEMARK

CAPSULES 250 mg. Bottles of 16, 100 and 1000

PEDIATRIC DROPS AQUEOUS 100 mg./cc. 1 Gm. in 10 cc. Plastic bottle

SYRUP 125 mg./5 cc. Bottles of 2 and 16 fl. oz.

Lederle LEDERLE LABORATORIES DIVISION
Cyanamid OF GREAT BRITAIN LTD., London, W.C.2

CYANAMID

This special shampoo

owes much of its success to the Medical Profession

Just about four years ago, Sebbix shampoo was introduced to the medical profession with marked success. Almost at once, doctors began to recommend Sebbix as a safe, sure means of controlling *pityriasis capitis*. Not until it had earned professional acceptance was Sebbix offered to the general public; and only then was it widely and carefully advertised. Today, Sebbix is a respected name in many households, and doctors continue to advise their patients to use this special shampoo—without the need of prescription. As a product which requires no prescription, Sebbix shampoo offers remarkable value both to private and N.H.S. patients. A point worth remembering.

Sebbix Shampoo eliminates dandruff

Liquid or Cream, 3/3. *Sachets*, 9d.

FORMULA

Hexachlorophane - - - - - - - 1%
*Purified Coal Tar Fractions - - - - 0.27%
*Designed to be therapeutically equivalent to 2% Crude Coal Tar.

A GENATOSAN PRODUCT

Diabetic Neuropathies

Complications involving the nervous system have long been recognized as a feature of diabetes. If the peripheral nerves are affected, administration of the whole vitamin B complex has been advocated. The therapeutic response to the entire B complex has been found to be considerably better than to thiamine alone. Although the parenteral route is recommended in the early stages of treatment, oral administration may be sufficient later.

Marmite yeast extract supplies all known factors of the vitamin B complex in a palatable form. It can be incorporated readily in the diabetic diet and, as it contains only a negligible quantity of carbohydrate, it need not be taken into the dietary calculations.

MARMITE

yeast extract

RIBOFLAVIN (*vitamin B_2*) 1.5 mg. per oz. NIACIN (*nicotinic acid*) 16.5 mg. per oz.

MARMITE LIMITED, 35, SEETHING LANE, LONDON, E.C.3. 5610

SILBEPHYLLINE

AN IMPROVED THEOPHYLLINE THERAPY

DIHYDROXYPROPYL-THEOPHYLLINE

soluble

neutral

stable

ADVANTAGES:

1 Intramuscular injections are **PAINLESS**.

2 Tablets do **NOT** produce nausea or gastric irritation.

3 Suppositories do **NOT** give rise to proctitis.

INDICATIONS: *Left ventricular failure. Congestive cardiac failure. Bronchial asthma.*

PACKINGS: *Ampoules, Suppositories and Tablets.*

SILBE

Samples and literature available on request.

SILTEN LTD · SILTEN HOUSE · HATFIELD · HERTS *Hatfield 3012*

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Haemorrhage from Anticoagulants

Q.—*What is the treatment for haemorrhage in patients who are on phenindione or similar anticoagulants?*

A.—Patients on prolonged anticoagulant treatment at home should carry two capsules of vitamin K_1 and take these with a drink of fruit juice immediately any bleeding is noticed. They should also carry an ampoule of vitamin K_1 for a doctor to inject if necessary. In addition, the patient must be instructed to stop taking the anticoagulant completely until he has a medical check-up and a blood test. The treatment is the accepted one and is preferable to blood transfusion, which may give rise to the production of undesirable circulating antibodies. Blood transfusion should be used only to replace blood loss when haemorrhage has been very severe. The sudden withdrawal of anticoagulant treatment and the rapid return of prothrombin levels to normal may, in certain cases, precipitate coronary thrombosis, but the dangers of this are negligible when measured against those of haemorrhage. Haemorrhage occurs only when the prothrombin levels are below 12% of normal, while anticoagulant action is still partly efficacious at 40% level. There is, therefore, usually time to assess the patient's condition before the danger level for thrombosis has been reached, and anticoagulant therapy may rapidly be restarted if bleeding has stopped.

Treatment of Anthrax, Botulism, and Snake-bite

Q.—*Where may emergency supplies of therapeutic and prophylactic agents for anthrax, botulism, and snake-bite be obtained in England and Wales?*

A.—A memorandum (H.M.(58)66) issued by the Ministry of Health in August lists the following centres as holding supplies of these agents. A 24-hour service is maintained at each centre.

Region 1: Newcastle.—The Pathological Laboratory, Cumberland Infirmary, Carlisle (anthrax antiserum and snake-bite antivenom only) (Carlisle 22332); The Dispensary, Newcastle General Hospital (Newcastle 38811).

Region 2: Leeds.—Castle Hill Hospital, Cottingham, Hull (Cottingham 47371); Seacroft Hospital, York Road, Leeds (Leeds 648164).

Region 3: Sheffield.—Nottingham City Hospital, Hucknall Road, Nottingham (Nottingham 63361).

Region 4: East Anglia.—Regional Transfusion Centre, Brooklands Avenue, Cambridge, Monday–Friday, 8.30 a.m.–5.30 p.m., and Saturday, 8.30 a.m.–12.30 p.m. (Cambridge 56912); all other times Cambridge 56913.

Region 5: North-west Metropolitan.—Edgware General Hospital (Edgware 2381).

Region 6: North-east Metropolitan.—North Middlesex Hospital, N.18: Day—Chief Pathologist, Night—Resident Pathologist (Edmonton 3071).

Region 7: South-east Metropolitan.—South London Transfusion Centre, South-east Sub-depot, David Salomon House, Southborough, near Tonbridge: day service (Southborough 1480); night service (Maidstone 4463 and 4660).

Region 8: South-west Metropolitan.—South London Transfusion Centre, Stanley Road, Sutton, Surrey (Vigilant 8221); Royal Portsmouth Hospital, Commercial Road, Portsmouth (snake-bite antivenom only) (Portsmouth 22281); *The Dispensary, Royal South Hants and Southampton Hospital (botulinus antitoxin and snake-bite antivenom only) (Southampton 26211); Royal Victoria Hospital, Shelley Road, Bournemouth (snake-bite antivenom only) (Boscombe 35201).

Region 9: Oxford.—Northampton General Hospital (Northampton 4680); Royal Berkshire Hospital, Reading (Reading 81721).

Region 10: South-western.—Ham Green Hospital, Bristol (Pill 2165); Pathological Department, Royal Devon and Exeter Hospital, Exeter (Exeter 73519; Exeter 72261 when laboratory closed); Scott Isolation Hospital, Plymouth (Plymouth 64311 and 61437); Pathological Department, Royal Cornwall Infirmary, Truro (Truro 3029).

Region 11: Wales.—Cardiff Isolation Hospital, Cardiff (Cardiff 21466); West Wales General Hospital, Glangwili, Carmarthen (botulinus antitoxin and snake-bite antivenom only) (Carmarthen 6733); Aberystwyth General Hospital (botulinus antitoxin and snake-bite antivenom only) (Aberystwyth 374); Caernarvon and Anglesey General Hospital, Bangor (botulinus antitoxin and snake-bite antivenom only) (Bangor 3321–5); Maelor General Hospital, Wrexham (Wrexham 3512).

Region 12: Birmingham.—The Dispensary, Selly Oak Hospital, Birmingham (Selly Oak 1361).

Region 13: Manchester.—The Dispensary, Manchester Royal Infirmary (Ardwick 3300).

Region 14: Liverpool.—Fazakerley Hospital, Longmoor Lane, Liverpool, 9 (Aintree 2342).

Anthrax antiserum for use prophylactically

Antiserum required for persons exposed to infection may also be obtained in 10-ml. containers during the day-time from the following centres:

Region 1: Newcastle.—Public Health Laboratory, Institute of Pathology, General Hospital, Westgate Road, Newcastle, 4 (Newcastle 38811).

Region 2: Public Health Laboratory, 16/18, Edmund Street, Bradford, 5 (Bradford 24314); Public Health Laboratory, 184, High Street, Kingston-upon-Hull (Hull Central 35371).

Region 5: North-west Metropolitan.—Central Public Health Laboratory, Colindale Avenue, London, N.W.9 (Colindale 7041).

Region 9: Oxford.—Public Health Laboratory, General Hospital, Northampton (Northampton 347).

Region 10: South-western.—Public Health Laboratory, Musgrove Park Hospital, Taunton (Taunton 5753).

Region 11: Wales.—Public Health Laboratory, Institute of Preventive Medicine, The Parade, Cardiff (Cardiff 29110 and 23967).

Region 12: Birmingham.—Public Health Laboratory, Royal Infirmary, Worcester (Worcester 5238/9).

Region 14: Liverpool, Public Health.—Laboratory, 126, Mount Pleasant, Liverpool (Royal 3636).

Pregnancy and Hodgkin's Disease

Q.—*What is the effect of pregnancy on Hodgkin's disease and on leukaemia?*

A.—There is no evidence that pregnancy has any adverse or beneficial effect upon the course of either Hodgkin's disease or leukaemia. 306 pregnancies occurring in 229 patients with Hodgkin's disease have been reported in the literature. Myles[1] analysed all the reported cases and showed that the relapse rate was no greater than that expected over a nine-month period in non-pregnant patients. Southam *et al.*[2] concluded from their own series that pregnancy probably does not alter the course of Hodgkin's disease. However, disease first manifest during a pregnancy tends to be more acute.

Sheehy[3] reviewed the course of chronic granulocytic leukaemia in 94 patients in whom an associated pregnancy had been reported. He found no significant difference in survival from a similar group without pregnancies. Yahia, Hyman, and Phillips[4] analysed 73 cases of acute leukaemia associated with pregnancy. Abortion or premature labour were common, but the course of the disease was not apparently affected. Very few cases of pregnancy occurring during the course of chronic lymphocytic leukaemia have been reported, probably because the age of onset of this type of leukaemia is most commonly post-menopausal and because the disease is in any case less common in women.

REFERENCES

1 Myles, T. J. M., *J. Obstet. Gynaec. Brit. Emp.*, 1955, **62**, 884.
2 Southam, C. M., Diamond, H. D., and Craver, L. F., *Cancer*, 1956, **9**, 1141.
3 Sheehy, T. W., *Amer. J. Obstet. Gynec.*, 1958, **75**, 788.
4 Yahia, C., Hyman, G. A., and Phillips, L. L., *Obstet. gynec. Surv.*, 1958, **13**, 1.

* This hospital carries snake-bite antivenom not only against native snakes but against tropical snakes which may be imported with cargoes arriving at the docks.

NOTES AND COMMENTS

Mortality from Whooping-cough.—Dr. PAUL DE BELLEFEUILLE (Ottawa, Ontario, Canada) writes: Many paediatricians will differ with the answer on mortality from whooping-cough ("Any Questions?" August 30, p. 574) on the matter of treatment. In the convulsant child "lumbar puncture is certainly useless." Perhaps, but I have seen protracted convulsing cease immediately upon relieving pressure thus. In the answer antibiotics are advised only in the treatment of secondary infection; in fact, whooping-cough itself, especially when seen fairly early, responds well to streptomycin, the tetracyclines, and chloramphenicol (the latter is perhaps preferred), and such therapy should not be withheld from the infant whooper. But even more important is serum therapy, using either human hyperimmune serum or rabbit hyperimmune serum, whereby death in infancy and troublesome bronchial disability in the future may be avoided. The last statement in the answer, on the uselessness of vaccine therapy once an attack has developed, should be modified by adding that an injection of vaccine to a child who has previously been vaccinated will have an early "booster" effect and help the child in fighting the infection.

OUR EXPERT replies: In a carefully controlled trial, conducted by the Medical Research Council,[1] chloramphenicol and chlortetracycline were both shown to have a slight beneficial effect in whooping-cough provided they were given in the first eight days of the disease—i.e., often before the whoop had developed. After this stage they were shown to have no effect and they should therefore not be given as a routine to children suffering from whooping-cough. They are perhaps best used in contacts of obvious cases when the disease can be suspected in the pre-whooping stage. The pathology underlying the severe type of convulsions is complex and the cerebrospinal fluid pressure is not always raised. Convulsions which clear up following a lumbar puncture can scarcely be due to the severe brain damage, which often causes coma lasting for weeks, if not death: probably every patient has a lumbar puncture carried out by a house officer, but the writer bases his opinion of its uselessness on over 20 years' experience of such cases. It would be difficult to prove that hyperimmune serum prevents death or future pulmonary disability without a control trial on a vast scale, for, after all, death is a comparative rarity in whooping-cough and future pulmonary disability very difficult to assess. Results from small published trials seemed to indicate that it might have some effect given early in young infants, but its effect was probably less conclusive than the effect of antibiotics already mentioned. With regard to the use of a booster dose of vaccine to children already immunized, surely the natural infection with live *H. pertussis* provided by an attack of the disease would be at least as potent a booster as an injection of dead vaccine. A large number of doubtful remedies for whooping-cough have been tried over the years with varying degrees of enthusiasm. I tried in my answer to give realistic suggestions for the prevention and treatment of the causes of mortality from the disease.

REFERENCE

[1] Medical Research Council, *Lancet*, 1953, **1**, 1109.

Extra Skin Crease.—Dr. R. D. LAURENSON (Kingston, Ontario, Canada) writes: Congenital dislocation of the hip is once more being discussed (*Journal*, June 14, p. 1432; July 5, p. 58; September 20, pp. 743 and 753). Interest is centred on the early diagnosis of this condition because delay in diagnosis so frequently leaves a tragic aftermath. It so happens that I have just completed a review of the literature on this subject in order to establish a background for further investigations into its aetiology. As a result of my findings, I consider the reply by your expert to the comment of Mr. H. H. Nixon ("Notes and Comments," September 20, p. 753) to be worth more than just a corner of a page. Your expert states: "Abnormal skin creases and limited abduction are in themselves not infallible but are certainly most suspicious." Exactly so. They are the very signs which may encourage a doctor to seek the guidance of an experienced orthopaedic surgeon. From my recent studies I am certain that to cast away any sign which may lead to an early diagnosis of congenital dislocation of the hip would be sheer folly.

Mr. H. H. NIXON (London, W.1) writes: I would like to take up a few points arising from your expert's reply to my letter ("Notes and Comments," September 20, p. 753). I agree wholeheartedly that everything possible should be done to diagnose congenital dislocation of the hip as early as possible. I still maintain that asymmetry of skin creases is an unsuitable test and that limitation of abduction is more suitable. The two cases your expert mentions from Caffey's paper[1] did indeed have normal abduction at first and yet subluxated later. He did not mention that they also had asymmetric skin creases so that neither test would have discovered them. I am not surprised at this, because his radiographs show that the subluxation was not present either. When it developed so did its physical signs. Early tests can be expected only to diagnose congenital dislocations. Post-natal dislocation will still need to be sought later. The relative frequency of these types is not yet known. Nor is there any reliable criterion of "dysplasia" or the inherited potential dislocation. Regarding the 44.2% of babies with limitation of abduction in Caffey's figures, it should be noted that most of them were slight limitations and that only 8.2% had limitation to 60% and only 3.8% had unequal limitation. In my experience the limitation in cases of congenital dislocation has been marked. It has been my practice to have *x*-rays of all such cases. In milder degrees of limitation the mother has been shown abduction exercises and the child seen again in three months. If the condition is simply what Denis Browne calls an asymmetric pelvis then abduction will have become freer. If it were a dislocation then persistence of the limitation would lead to an *x*-ray which would reveal it without undue loss of time. In fact, none of these milder asymmetries has yet proved to have a dislocation. Dr. E. Loewenstein-Kuester's letter (*Journal*, September 20, p. 743) reminds us how important this condition is. My anxiety is that enthusiasm may lead to a spate of unnecessary (and not necessarily harmless) pelvic radiography, and even unnecessary treatment of alleged "preluxations."

REFERENCE

[1] Caffey, J., Ames, R., Silverman, W. A., Ryder, C. T., and Hough, G. *Pediatrics*, 1956, **17**, 632.

OUR EXPERT replies: The further comments of Mr. Nixon and of Dr. Laurenson are of interest. It is appreciated that there are difficulties, but, like Dr. Laurenson, I feel that the occasional abnormal skin crease is an indication for examination, and if necessary radiology, to avoid the tragedy of late diagnosis of congenital dislocation of the hip.

Corrections.—Dr. M. J. TARSH writes: My attention has been drawn to certain historical inaccuracies in my summary of the background of the Hebrew University Medical School (*Journal*, September 6, p. 605). The British Mandate in fact ended on May 14, 1948, and not in 1947. Mr. Ben Gurion declared the existence of the State of Israel on the next day. The "year of intermittent fighting" that I mentioned took place immediately from this date and is usually referred to as "The War of Liberation." The combined Arab attack to which I referred started also on May 15, 1948. Mount Scopus was and still is an area of great strategic importance.

There was a mistake in Figure 1 in the article entitled "The Physiological Activity of D-Thyroxine" by Dr. Raymond Greene and Miss Helen E. A. Farran (November 1, p. 1057): under "Dosage," in the bottom right-hand corner of the figure, the squares denoting L-thyroxine and D-thyroxine should be transposed.

In the article "Rationale of Antihistaminic Therapy in Thermal Injury," by Drs. D. L. Wilhelm and Miss Brenda Mason (*Journal*, November 8, p. 1141), line 31 of the first column on page 1142 should read "... was graded ±, ±, +, +±, ++," and the last line of the first column on page 1142 should read "... as little as 10 μg./kg. to ± (Fig. 1)."

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

Emergencies in General Practice (26s. 9d.).

Refresher Course for General Practitioners, Volumes 2 and 3 (26s. 9d.).

Clinical Pathology in General Practice (22s. 3d.).

Any Questions?, Volumes 2 and 3 (8s. 3d. each).

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.

ADVERTISEMENTS should be addressed to the Advertisement Director, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 4499. TELEGRAMS: *Britmedads, Westcent, London.*

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association. TELEPHONE: EUSTON 4499. TELEGRAMS: *Medisecra, Westcent, London.*

B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.